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A STUDY OF AQUEOUS SOLUTIONS OF ACETIC ACID BY THE METHOD OF RAMAN SPECTRA

A. A. Glagoleva and A. A. Ferkhmin

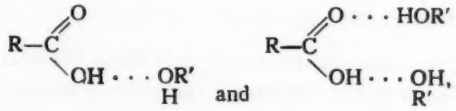
Some organic acids play a very important role in the living organism; however, their concentration in the latter is very small, and consequently their study encounters great difficulties. We decided to study the organic acids of greatest biological interest by the method of Raman spectra. The first acid taken by us for study was acetic acid as being the acid most studied by various methods. Despite this, many disputes have arisen regarding the change in the structure of acetic acid when the latter is diluted with water. Many different opinions also exist on the formation of hydrates.

Since previous investigations dealt mainly with high concentrations, we began our study with solutions of high concentration, gradually diluting them with water.

Most authors assume that acetic acid shows association into dimers [1-6]. Pauling and Brockway [7] showed that formic acid representsdimers in the form of closed rings. Huggins [8] expressed the theory that the dimers of monobasic acids are closed by two hydrogen bridges into a ring. Many assume that the ring dimers of monobasic acids suffer decomposition in polar solvents, like for example water, being converted on great dilution into monomers [9-12]. Some authors postulate that in liquid acetic acid, besides ring dimers, there is also present a certain amount of monomers and open dimers (for example, [6]). Huggins [8] indicates that liquid formic acid can, together with dimers, also form chain polymers composed of a large number of acid molecules. Batuev [13-15] postulates that the latter is also true for the acetic acid molecule.

Contradictory opinions also exist on the possibility of forming hydrates in aqueous solutions of aliphatic acids. Jones [1] and Koteswaram [16] rejected the formation of hydrates. The majority of the authors [6, 8, 13-25] who studied these acids believe that hydrates are formed. Some authors indicate that dihydrates can also arise [6, 8, 19-24].

Recently a paper by Izmailov and Kutsyna [25] appeared, in which it is indicated that the behavior of carboxylic acids in solutions of monohydric alcohols is the same as it is in water. Two structures are given by them:



corresponding to the mono- and dihydrate of the acid molecule in water.

In order to determine in more detail the behavior of acetic acid solutions in water, and mainly to study more dilute solutions, we investigated a large number of concentrations by the method of Raman spectra.

The microphotometric curves for various concentrations are shown in Figs. 1-3. The Raman spectra were taken using an ISP-51 spectrograph with a glass light filter, isolating the mercury line 436 mμ. An MF-2 microphotometer was used to obtain the microphotometric curves. An IZA-2 comparator was used to measure the frequencies. For convenience the microphotometric curves were divided into three parts: in Fig. 1, from 900 to 1900 cm^{-1}; in Fig. 3, from 150 to 1000 cm^{-1}; and in Fig. 4, from 2800 to 3750 cm^{-1}.

Passing over to a description of the microphotometric curves, we will first discuss the band most sensitive to a change in the concentration, namely, the band corresponding to the C=O bond (Fig. 1); this band also appears to be the most studied [5, 6, 10, 11, 14-17, 26-36].

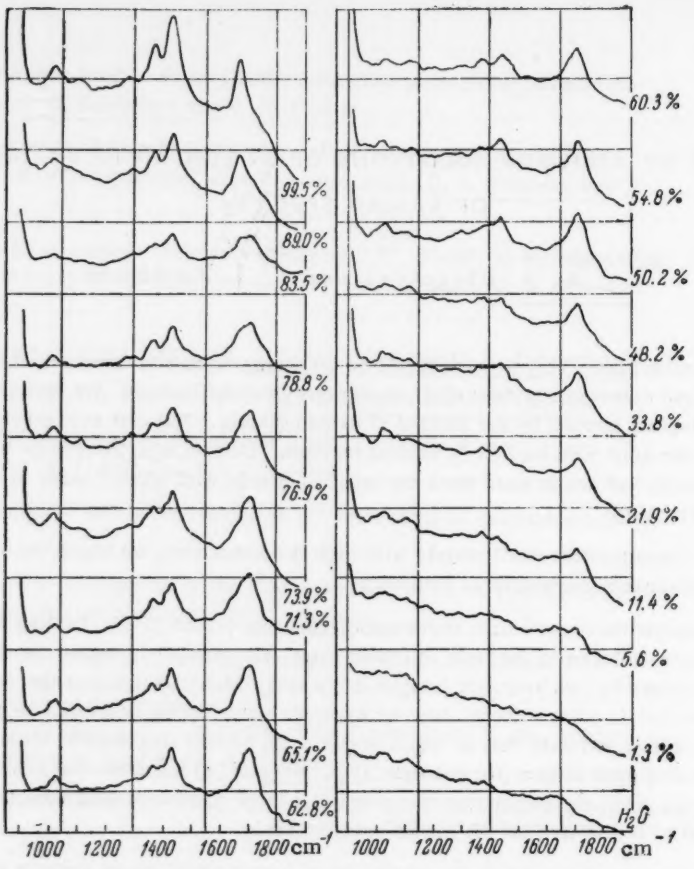
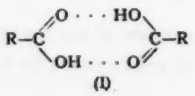


Fig. 1. Change in the Raman spectrum as a function of the concentration of acetic acid in aqueous solution ($\Delta\nu$ 900-1900 cm^{-1}).

In order to obtain an easier understanding of what happens with this band, we will utilize the table given below. In the 1st column of this table we give the concentrations of the acid in weight percent, in the 2nd column – in mole percent, in the 3rd – the most intense bands for the corresponding concentration, in the 4th – the bands with approximately the same intensity, and in columns 5-8 – the bands with weak intensity. The lines of the light source may be superimposed on the latter (Fig. 2).

According to the literature data, concentrated acetic acid shows bands at 1660 cm^{-1} (most intense), 1700-1710 and 1740 cm^{-1} (both of the latter being weak). As was shown by many authors, the band at 1660 cm^{-1} belongs to the ring dimer of type (I).



(I)

The presence of the 1700 and 1740 cm^{-1} lines suggests that open dimers [6] could also be present, but in small amount. Batuev [13] believes that these lines belong to higher polymers.

According to our investigations, in 99.5% acetic acid solution the band of the carbonyl group is relatively

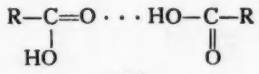
narrow, with a well-defined maximum at 1660 cm^{-1}; the remaining maxima of the band are weakly expressed (Fig. 1).

TABLE

Change in the Frequency of the C=O Group as a Function of the Concentration of Acetic Acid Solutions

Concentration		(in cm^{-1})					
(in wt. %)	(in mole %)						
1	2	3	4	5	6	7	8
99.5	1.66	1660	1700	1635			1755
89.0	1.48	1660	1700	1625			1740
83.5	1.39	1697	1665	1640			1745
78.8	1.31	1697	1690, 1667	1635			1745
76.9	1.28	1700	1687	1650. 1630			
73.9	1.23	1700		1650. 1620			1750
71.3	1.19	1700		1640			1750
65.1	1.08	1700	1680	1640			1760
62.8	1.05	1700	1690	1640			1755
60.3	1.00	1700	1690		1665		1750
54.8	0.91	1700	1690	1645. 1620	1675		1750
50.2	0.84	1700	1690	1640		1725	
48.2	0.80	1700	1690	1635			1745
33.8	0.56	1700		1645. 1625	1675		1740
21.9	0.36	1700	1695	1655			
11.4	0.19	1700		1630	1675		1765
5.6	0.09	1695	1705	1653. 1625		1720	1765
1.3	0.02	1695	1705	1652. 1620. 1640	1675	1725	1760. 1767
H_2O	—	—	—	1630	—	—	—

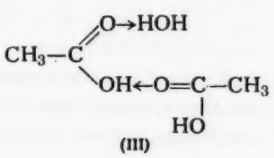
At 89.0% acid the 1660 cm^{-1} band continues to remain quite intense, but the maximum at 1700 cm^{-1} begins to get stronger. As a result of this the band becomes broader. It is very probable that quite a large number of open dimers are found present at this solution concentration, but without doubt the ring dimers still predominate. Further dilution with water leads to an increase in the number of dimers present as chainlets (II).



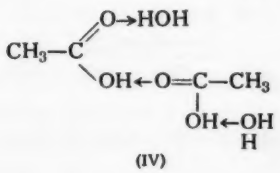
(II)

At a concentration of 83.5% the 1697 and 1665 cm^{-1} bands have nearly the same intensity; then the 1697 cm^{-1} band becomes more intense, while the 1665 cm^{-1} band becomes weaker (a shift of the band at 1660 to 1665, and of the band at 1770 to 1697 cm^{-1}, is explained by the mutual influence exerted by these bands on each other due to the small dispersion of the spectrograph).

At a concentration of 78.8% the line at 1667 cm^{-1} is still clearly seen; consequently, here a substantial number of ring dimers are contained in the solution. A new band appears at 1690 cm^{-1}. It is possible to assume that in this region of concentrations the water first adds according to schemes (III) and (IV), given by Murty and Seshadri [6].



(III)

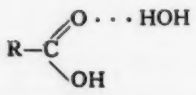


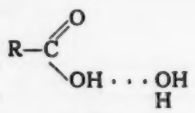
(IV)

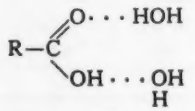
At a concentration of 76.9% the band at 1700 cm^{-1} becomes narrower and the maximum at 1667 cm^{-1} dis-

appears. Consequently, if any ring dimers did remain, then they are present in such small amount that it is difficult to detect them. Some authors [6, 17, 21-24] have shown the formation of the monohydrate at this concentration of acid.

With further dilution, and specifically at an acid content of 73.9 and 71.3%, special changes in the configuration of the band at 1700 cm^{-1} fail to be observed. At this concentration there still remain some monohydrates as chain dimers, and as some authors believe, the chain dimers suffer cleavage with the formation of hydrates of the type of (V) and (VI) and subsequent formation of dihydrates of the type of (VII).


(V)


(VI)


(VII)

At a concentration of 65.1 and 62.8%, the band corresponding to the C=O group becomes sharper and narrower; according to the data of [21-24], dihydrates are formed in this region of concentrations.

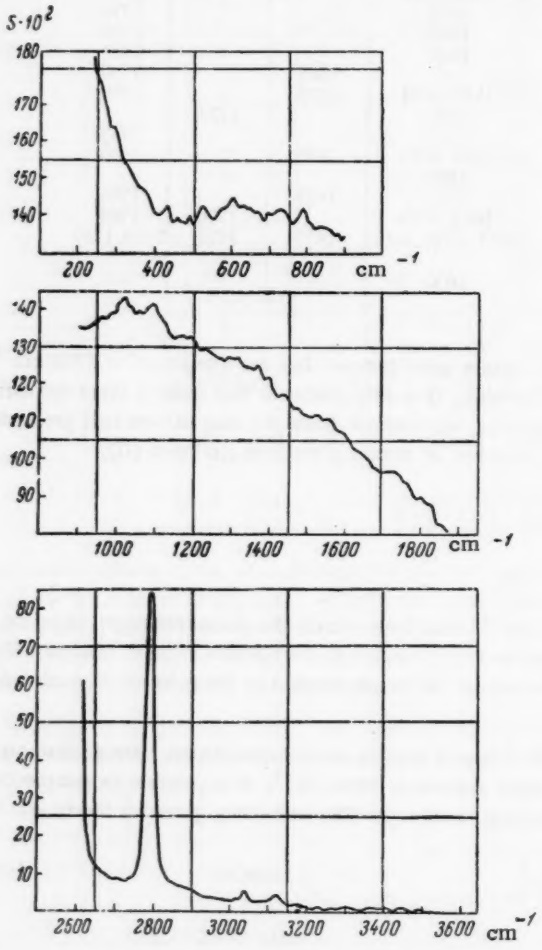


Fig. 2. Microphotometric spectral curve of a PRK-2 mercury lamp.

Beginning with a concentration of 60.3% a line appears at 1670 cm^{-1}. Apparently, this line belongs to the light source, since at low concentrations the lines of the light source steadily become more noticeable. It is possible that the bands at 1720 and 1750 cm^{-1} also belong to the light source. In any case, close maxima exist on the microphotometric spectral curve of the light source (Fig. 2). Unfortunately, we were unable to utilize the so-called "cold" mercury lamp.

With further dilution the maximum of the band, belonging to the C=O group, hardly changes and only its relative intensity gradually diminishes. It exists even down to 1.3%. At these concentrations a maximum is also seen at 1690 cm^{-1}.

In our opinion the band at 1690 cm^{-1} in acetic acid solution belongs to the C=O group to which the water had added through hydrogen bonding. Since this same maximum is also seen at an acetic acid concentration of 1.3%, it is possible to postulate that the bond with water in the carbonyl group continues to exist at least down to this concentration, where the amount of ions present is still very small.

From Fig. 1 it can be seen that the general maximum at 1700 cm^{-1}, beginning with a concentration of 78.8% and lower, in acetic acid solutions does not change its position. Most authors believe that it shifts with dilution toward greater frequencies. To be sure, there is hardly any data in the literature for concentrations below 20% and no systematic studies of solutions with close concentrations.

We will pass over to a description of the band at 1430 cm^{-1}. Different opinions exist as to which group is responsible for this band. Some authors [12, 16, 37] believe that it belongs to the CH_2 group. According to the data of [31], it disappears when a hydrogen in the CH_3 radical is replaced by deuterium. Edsall [32], however, believes that this frequency belongs to the carboxyl group. According to our data, it fails to shift clear down to a concentration of 1.3%, but beginning with 83.5%, additional maxima appear. It is possible to assume that this frequency at 1430 cm^{-1} belongs to either the C–O or the C–OH group (according to Karle and Brockway [33], the distance between atoms for C=O in the dimer is 1.25 A, and for C–O this distance is 1.36 A; consequently, the frequency for C–O should be smaller than for C=O).

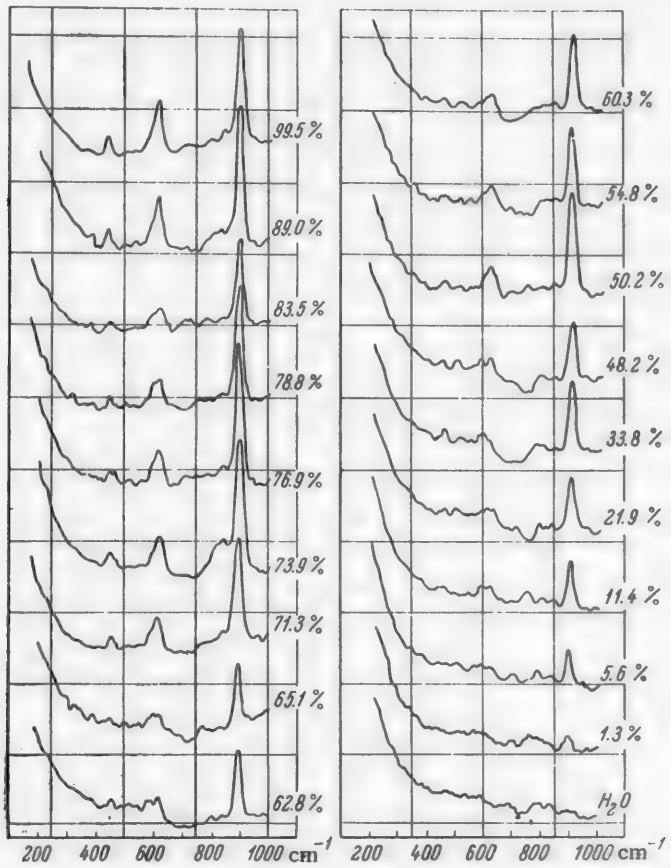


Fig. 3. Change in the Raman spectrum as a function of the concentration of aqueous acetic acid solutions ($\Delta\nu$ 150-1000 cm^{-1}).

The appearance of an additional maximum at lower frequencies can apparently be explained by a rupture of the ring dimer and the formation of the monohydrate. With further dilution, where in our opinion the formation of monomers (V) and (VI) and the further addition of water to yield the dihydrate (VII) occurs, the shift of the frequency gradually increases, as was to be expected. The 1430 cm^{-1} frequency exists in the spectrum of acetic anhydride [31]. This speaks against its belonging to the C–OH group. This same band is also present in the spectra of methyl and ethyl alcohols, but it is shifted toward greater frequencies.

Venkateswaran and Bhagavantam [28] considered the frequency at 1360 cm^{-1} as belonging to the C–OH group, since a band close to this is found in the alcohols. Other authors attributed it to the CH_3 group. The latter seems invalid to us, since, beginning with 48.2%, it disappears (which could not be if it belonged to the radical), and in place of it bands appear at 1345 and 1370 cm^{-1}, which possibly belong to the light source (Fig. 2). This can also be seen from Fig. 6, where the curves for dilute solutions are shown in greater detail (the photographs were taken on different plates). These bands, especially the band at 1370 cm^{-1}, are quite intense in the spectrum

of water. It should be mentioned that the band at 1360 cm^{-1} is also present, with hardly any changes, in the spectrum of acetic anhydride [31]. Saksena [11] attributes the band at 1360 cm^{-1} to the symmetrical vibration of the carboxyl group.

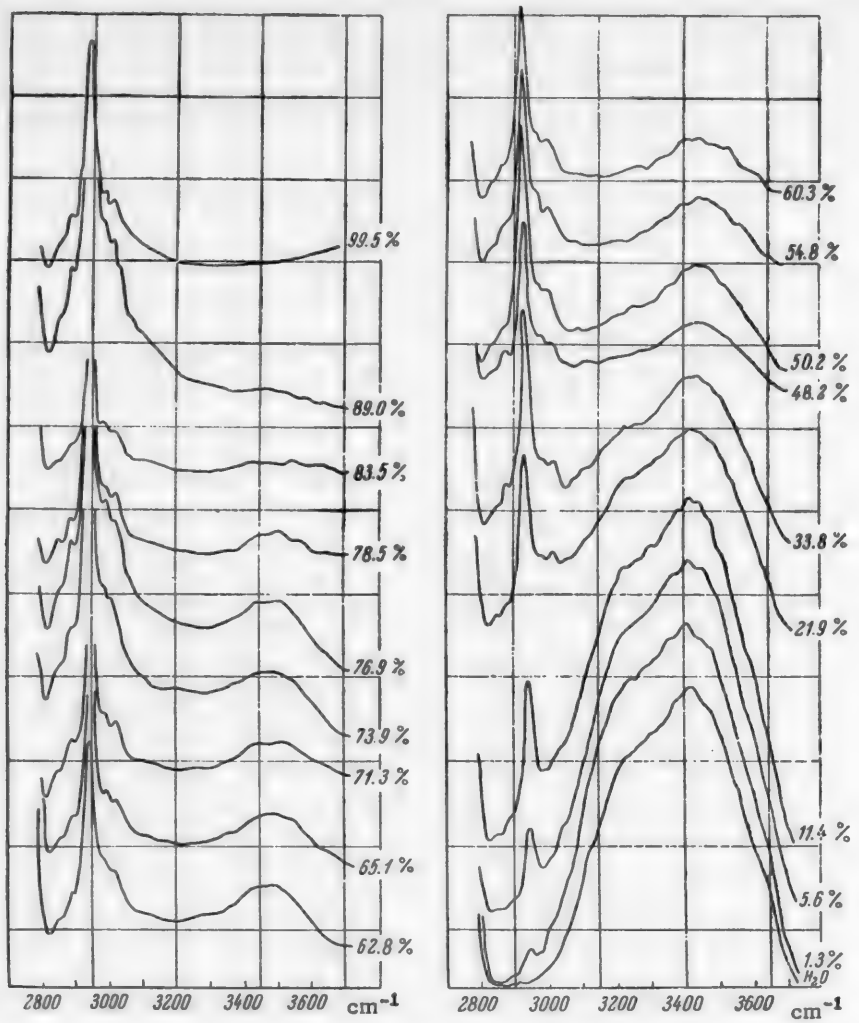


Fig. 4. Change in the Ramanspectrum as a function of the concentration of acetic acid in water solution ($\Delta\nu$ 2800-3750 cm^{-1}).

It is difficult to say anything about the lines in the frequency region 1250-1000 cm^{-1}. Some authors [28, 31] attributed the line at 1010 cm^{-1} to the deformation vibration of the carboxyl group. It is difficult to decipher these frequencies, since quite intense lines of the light source exist in this frequency region, and in character they resemble very closely the bands found in the spectrum of acetic acid (cf. Figs. 1 and 2). When the acid is diluted the intensity of these lines increases when compared with the other bands. Pure water also gives these bands. We believe that they are not attributable to acetic acid.

We will pass over to a discussion of Fig. 3. The most intense line on this figure is at 892 cm^{-1}. There are no special arguments relative to its origin. It is assumed to belong to the C—C bond [16, 28, 30]. This band completely fails to change in either position or contour on dilution and is still present at a concentration of 1.3%. To be sure, at this concentration it appears complex, but this complexity is only apparent, since the bands found in the spectrum of water or those of the light source are also present in the given region.

Of great interest is the behavior shown by the next most intense band at 617 cm^{-1}. It has a simple structure

only in concentrated acetic acid (99.5%). Beginning with 89.0%, this band becomes broader due to an additional maximum on the side of the frequencies below 600 cm^{-1}, on dilution shifting to 590 cm^{-1}; this maximum remains when the acid concentration is decreased further. In the concentration region 65-60% acid a second maximum appears that is due to even smaller frequencies, and specifically at 580 cm^{-1}. On dilution the band at 590 cm^{-1} steadily becomes more noticeable, increasing in intensity when compared to the band at 617 cm^{-1}. At a concentration of 33.8% the bands at 617 and 590 cm^{-1} show almost the same intensity (cf. also Fig. 5), and at a concentration of 5.6% the intensity of the band at 590 cm^{-1} even predominates.

A special study of this band at 590 cm^{-1} was made by Leitman and Ukhodin [38], who studied the change in its intensity when the acid was diluted with water. According to their data, the intensity is greatly weakened at a concentration of 40%. This is in agreement with our data. Saksena [11], the same as Leitman and Ukhodin, believes that this band is attributable to association of the molecule (for trichloroacetic acid). According to the data of many authors, this band is absent in alcohols (cf., for example [39]) and in oxalic acid. It is also known [31] that this frequency changes when only the hydrogen atom in the carboxyl group of the acid is replaced by deuterium. Sverdlov [36] attributes this frequency to the deformation vibration of O–C–O.

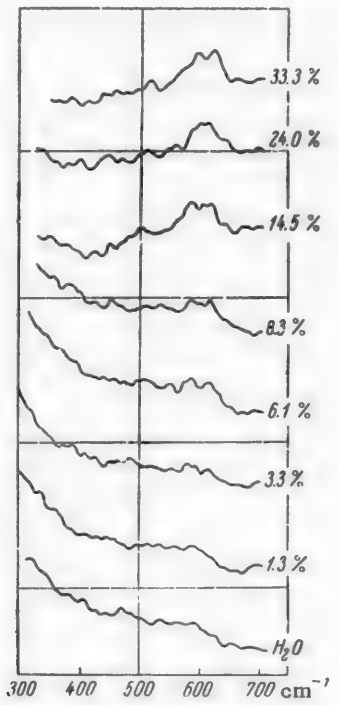


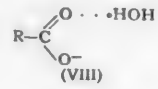
Fig. 5. Change in the Raman spectrum as a function of the concentration for aqueous acetic acid solutions ranging in concentration from 33.3 to 1.3%.

The behavior of this frequency is comparable to that of the C=O band, which changes with change in the hydrogen bonding in the acid on rupture of the ring dimer and in the formation of hydrates.

The band at 445 cm^{-1} also shows strong change with change in the acid concentration. Thus, at 99.5% it, the same as the band at 617 cm^{-1}, fails to have a complex structure. Beginning with a concentration of 89.0%, an additional maximum appears, but only its frequency is greater, being found at 460 cm^{-1}. This maximum is retained on further dilution. However, in the more dilute solutions a relatively intense maximum appears at 435 cm^{-1}. This band also changes its structure on dilution of the acid with water. An extremely intense band, shown in Fig. 4, appears at 2944 cm^{-1}; it belongs, as has been shown by a very large number of authors, to the CH_3 group. This band is complex: it also contains three weaker bands at 2880, 2990 and 3023 cm^{-1}. It is possible for the 5026 A mercury line (3046 cm^{-1} in the Raman spectrum) to be superimposed on the last band. All of these bands are quite fixed in their position. They can be seen clear down to an acetic acid concentration of 1.3%. The statement made by Batuev [15, 40] that the bands at 2990 and 3023 cm^{-1} belong to the frequency of the O–H group in the dimeric ring seems improbable, since it completely fails to change its position with change in the concentration, despite the rupture of the rings and further transformations of the acetic acid molecule into monomers with greater dilution. In addition, Batuev believes that a broad band is present at dilutions of the order of 10%, belonging to the O–H group of the polymer. However, a superimposition of the O–H band on the 2944 cm^{-1} band and its components is not seen at a single concentration. A well-defined minimum exists between the CH_3 and O–H bands, while in general there are no bands or lines whatsoever in concentrated acid. A well-defined minimum is present in the 3100-3600 cm^{-1} region. It could be mentioned that the higher the concentration of the solution, the greater is the shift of the O–H band toward greater frequencies. For example, in the spectrum of water the maximum is at approximately 3430 cm^{-1}, while in the spectrum of 78.8% acid it is at approximately 3550 cm^{-1}. This is a known fact.

We will now pass over to a discussion of the spectra of solutions with a low concentration, since such solutions are of especial interest to us. We repeated the photographing of acetic acid solutions on new plates and at smaller concentration intervals (Figs. 5 and 6).

The band, corresponding to the C=O group, can be seen even at the very low concentrations studied by us. It can be shown at 1.3%. At 33.0% it is sharply defined and has a general maximum at 1700 cm^{-1}. Besides this maximum, there are also maxima at 1710 and 1680 cm^{-1}. On further dilution the band retains its position to approximately a concentration of 8.3%; then the maximum at 1700 cm^{-1} vanishes, and only the maxima at 1690 and 1710 cm^{-1} remain, which are retained down to a concentration of 1.3%. The presence of a band at 1690 cm^{-1} can serve as evidence that water remains attached to the C=O group for quite a long time, despite the fact that dissociation begins with a concentration of 6.0%. If it is assumed that the band at 1430 cm^{-1} corresponds to the C–O bond, then water begins to be cleaved at approximately 24.0%, (the maximum at 1420 cm^{-1} vanishes) which is quite probable in connection with the further formation of ions of the hydrated form (VIII).



(VIII)

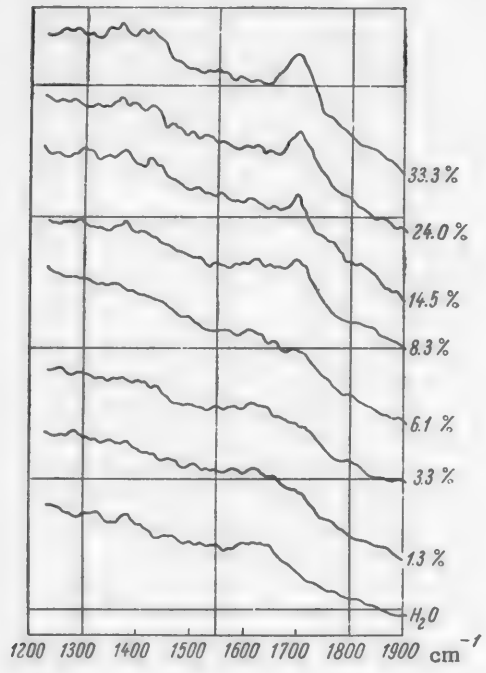


Fig. 6. Change in the Raman spectrum as a function of the concentration for aqueous acetic acid solutions ranging in concentration from 33.3 to 1.3%.

The band at 617 cm^{-1} in solutions of low concentration changes very strongly on dilution. At 33.3% it appears as a doublet (two maxima of of the same intensity at 617 and 590 cm^{-1}). There is also a hint of a third maximum at about 580 cm^{-1}, which becomes stronger with dilution. At 14.5% all three maxima have nearly the same intensity; then the maximum at 590 cm^{-1} begins to weaken and appears again at 1.3%. It is possible that in the spectra of solutions of very low concentration it is now due to the weak line of the light source. The band at 617 cm^{-1} can be seen down to a concentration of 3.3%.

SUMMARY

1. A study was made of the change in the Raman spectra of aqueous acetic acid solutions as a function of the concentration (from 99.5% down to 1.3%).

2. The appearance of a maximum 1690 cm^{-1} in the band of the carbonyl group is explained by the formation of hydrates of acetic acid.

3. A change in the configuration of the band at 617 cm^{-1} on dilution of the acid with water proceeds simultaneously with a change in the hydrogen bonding in the acid. The band does not have structures in the ring dimer; on rupture of one hydrogen bond a maximum appears at about 600 cm^{-1}, which on further dilution shifts to 590 cm^{-1}, while in the concentration region of 65-60% (formation of dihydrates) still another maximum appears (at 580 cm^{-1}). As a result, the appearance of the band at 617 cm^{-1} is linked to the molecular structure of the acid.

4. The band at 1430 cm^{-1} (and possibly the band at 1360 cm^{-1}) we regard as belonging to either the C–O group or to the C–OH of the carboxyl. In the ring dimer this band does not have a complex structure. It does not change its position on dilution of the acid with water, but with dilution an additional maximum appears at lower frequencies, the position and relative intensity of which changes with change in the concentration.

5. Beginning with 78.8% and on further dilution a shift of the band at 1700 cm^{-1}, corresponding to the carbonyl group, fails to occur. This band can be seen down to a concentration of 1.3%.

6. The group of bands at 2944, 2880, 2990 and 3023 cm^{-1} remains completely fixed and does change its position at all dilutions, clear down to a concentration of 1.3%. Consequently, these bands without doubt belong to the acetic acid radical.

7. The band at 892 cm^{-1}, belonging to the C–C bond, also does not change on dilution down to a concentration of 1.3%.

8. The groups of bands near 1020 and 1105 cm^{-1}, which some authors ascribed to acetic acid, apparently belong to the light source.

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TERNARY RECIPROCAL SYSTEM OF SODIUM AND POTASSIUM FORMATES AND NITRATES

O. I. Dmitrevskaia

A study of the reaction of the sodium and potassium salts of fatty acids with nitrates in melts was directed toward obtaining data on the influence of complex-formation on the exchange process, on the direction of the exchange reaction, and also to determine the influence exerted by the chain length of the hydrocarbon radical of the fatty acid salt on the character of exchange and complex-formation.

EXPERIMENTAL

Method of Operation. The visual polythermal method of physicochemical analysis was used to make the study. The temperature when the first crystals appeared was measured using a nichrome-constantan thermocouple. The salts of c.p. quality were recrystallized and dried to constant weight; they had the following melting points: HCOONa 258°, HCOOK 167°, KNO_3 337°, $NaNO_3$ 308°.

Transitions in the solid state were observed for all of the salts: KNO_3 – at 124 and 316° [1-3], $NaNO_3$ – at 270° [2-4], and HCOONa – at 242° [5]; HCOOK has three transitions in the solid state at 60, 135 and 157° [5].

All of the compositions are expressed in mole percent.

TABLE 1

Binary Systems

HCOONa–$NaNO_3$		HCOOK–KNO_3				HCOONa–HCOOK			
% $NaNO_3$	temp.	% KNO_3	temp.	% KNO_3	temp.	% HCOOK	temp.	% HCOOK	temp.
0	258°	0	167°	50	172°	0	258°	65	179°
10	242	5	166	55	193	5	252	70	180
15	232	10	165	60	212	10	246	75	182
25	214	15	164	65	230	15	240	80	181
35	198	20	162	70	248	20	232	85	179
40	192	25	159	75	264	25	222	90	173
45	188	30	155	80	279	30	209	96	167
49	186	32.5	150	85	294	35	198	97	168
50	190	35	153	90	309	40	186	98	171
55	206	37.5	154	95	323	45	176	99	169
65	235	40	150.5	100	337	49.5	168	99.5	168
75	262	42	146	—	—	50	169	100	167
85	284	45	153	—	—	55	172	—	—
100	308	47.5	161	—	—	60	176	—	—

Binary Systems. 1. System HCOOK–KNO_3 was studied first. Here the compound $2HCOOK \cdot KNO_3$ is formed, which forms eutectics with the original components: at 150° and 67.5% HCOOK, and at 146° and 44% KNO_3 (Table 1, Fig. 1).

2. System HCOONa–$NaNO_3$ had been studied earlier [6]; it forms a eutectic at 186° and 49% $NaNO_3$ (Table 1, Fig. 1).

3. System HCOOK–HCOONa was studied by us for the first time; the compound 3HCOOK · HCOONa is formed here, which with the original components gives eutectics at 168° and 49.5% HCOOK, and at 167° and 4% HCOONa (Table 1, Fig. 1).

4. System $NaNO_3$–KNO_3 has been studied by many authors [2, 7-10], and we utilized the data given in [2]. A continuous series of solid solutions is formed in this system with a melting point minimum at 223° and 50% KNO_3 (Fig. 1.).

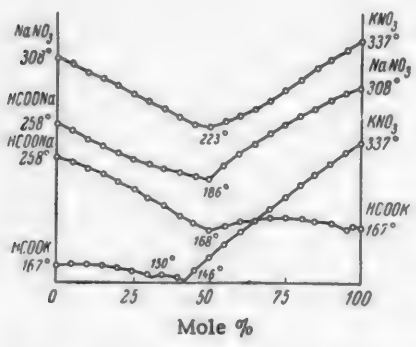

Fig. 1. Fusion diagram of binary systems.

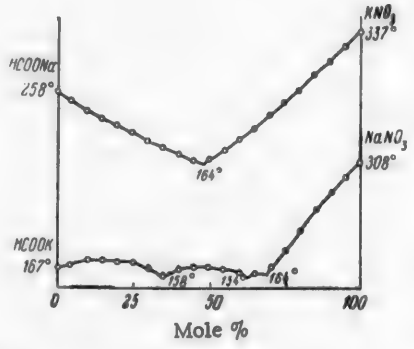

Fig. 2. Fusion diagram of diagonal sections.

Diagonal Sections. 1. HCOONa–KNO_3 is a stable diagonal with eutectic point at 164° and 48% KNO_3. The polymorphous transformation of HCOONa, discovered by N. M. Sokolov [5], is observed on the HCOONa branch at 242°. The KNO_3 branch is curved somewhat under the influence of solid solutions Na, K ‖ NO_3 (Table 2, Fig. 2).

2. HCOOK–$NaNO_3$ is an unstable diagonal. The fusion curve has four branches of crystallization, intersecting in three points: at 158° and 34.5% $NaNO_3$, at 155° and 63% $NaNO_3$, and at 164° and 69% $NaNO_3$ (Table 2, Fig. 2).

TABLE 2

Diagonal Sections

Stable						Unstable					
HCOONa–KNO_3						HCOOK–$NaNO_3$					
% KNO_3	temp.	% KNO_3	temp.	% KNO_3	temp.	% $NaNO_3$	temp.	% $NaNO_3$	temp.	% $NaNO_3$	temp.
0	258°	35	188°	75	235°	0	167°	34.5	158°	65	158°
2.5	252	40	180	80	252	2.5	169	35	159	67.5	163
5	242	45	172	85	269	5	170	37.5	162	69	164
7.5	241	48.5	164	90	288	10	174	40	164	70	168
10	236	50	166	95	307	15	176	45	166	75	195
15	226	55	180	96.5	316	20	176	50	166	80	224
20	218	60	193	97.5	322	25	173	55	164	90	272
25	208	65	205	100	337	30	167	60	160	95	292
30	199	70	220	—	—	32.5	163	63	154	100	308

Fusion Diagram of Reciprocal System. Based on the results of studying the binary systems, and the diagonal and 23 internal sections (Figs. 3-6), we constructed a projection of the joint crystallization curves on the plane of the polytherm of the binary system $NaNO_3$–KNO_3 (Fig. 8); this made it possible to determine the positions of the ternary and isothermal points on the joint crystallization curves. A projection of the liquidus diagram of the ternary reciprocal system on the composition square, with the isotherms drawn at 20° intervals, is shown in Fig. 7. The system is irreversible-reciprocal with a stable diagonal, which agrees with the conditional heat effect (or the exchange reaction, equal to 3.37 kcal/equiv on the side of the stable pair HCOONa and KNO_3:

$$\underset{160.7}{HCOOK} + \underset{111.72}{NaNO_3} \longrightarrow \underset{157.7}{HCOONa} + \underset{118.09}{KNO_3}$$

The heats of formation were taken from a handbook [11]. Although the conditional thermochemical effect for the exchange reaction is small, and complex-formation occurs at the sides and inside the system, still the system belongs to the class of diagonal systems, and complex-formation does not change the direction of the exchange reaction.

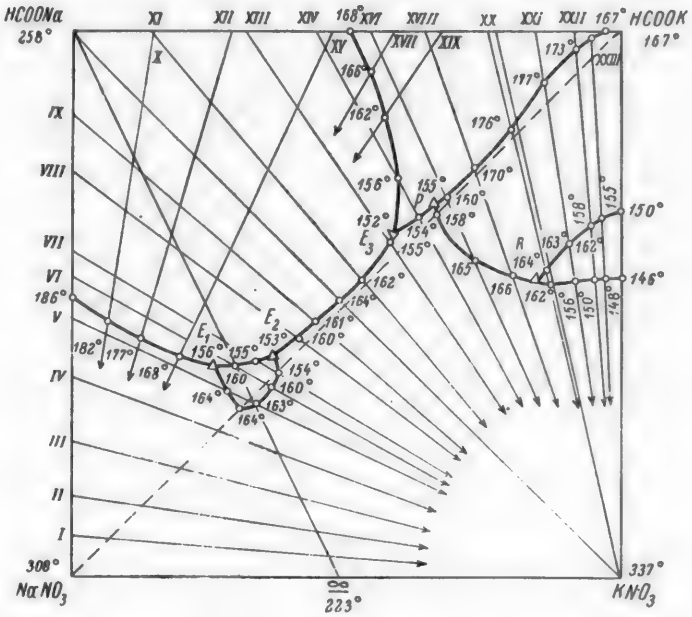

Fig. 3. Arrangment of internal sections in the reciprocal system Na, K‖NO_3, HCOO.

The compound 2HCOOK · KNO_3, formed on the HCOOK−KNO_3 side, tapers out in the reciprocal system and ceases to exist in the transition point R at 164°. The eutectics of the binary system HCOOK−KNO_3 have melting points that are below either the transition point or the melting point of the ternary eutectic. Point R in the reciprocal system is a point of double rise.

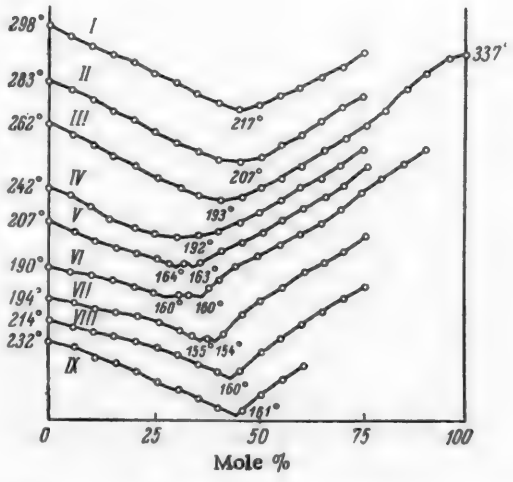

Fig. 4. Internal cross-sections of reciprocal systems I-IX.

The liquidus surface of the reciprocal system is divided into six crystallization fields: 1) field HCOONa, 2) field of the compound 3HCOOK HCOONa, 3) field HCOOK, 4) field of the compound 2HCOOK · KNO_3, 5) field of solid solutions Na, K ‖ NO_3, and 6) a field, apparently belonging to the compound $NaNO_3$ · KNO_3, which is formed, according to the data of A. G. Bergman, in the decomposition of solid solutions Na, K ‖ NO_3 when the temperature is lowered to 180°, while in the side system it appears very vaguely at 165-175° in the region of the solid state [14]. In the investigated system it appeared at 165°. Similar fields were also observed in the systems: Na, K ‖ NO_3, CH_3COO [12], Na, K ‖ NO_3, SO_4 [13] and Na, K ‖ NO_3, NO_2 [14], but under the stabilizing influence of the acetates and nitrates they appeared on the liquidus surface at a higher temperature; it is obvious that the formates failed to show a stabilizing influence in the investigated system.

The compound 3HCOOK · HCOONa, congruent on the binary side HCOOK–HCOONa, becomes incongruent in the reciprocal system. Triangulation of the system is accomplished by the stable diagonal HCOONa–KNO_3 (stable cross section) and two unstable cross sections: one starts from the zone of the compound $NaNO_3$ · KNO_3 and goes to the HCOONa vertex, while the other starts from the zone of the compound 3HCOOK · HCOONa and goes to the KNO_3 vertex.

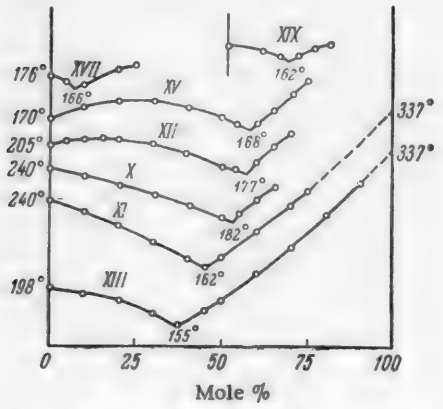

Fig. 5. Internal cross-sections of reciprocal systems X–XIII, XV, XVII and XIX.

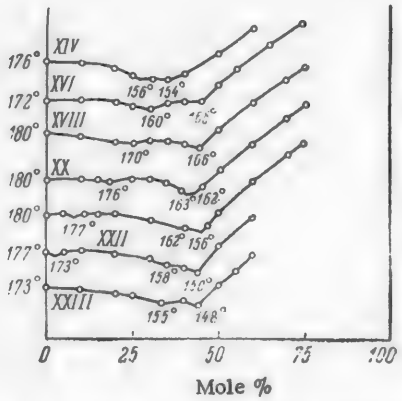

Fig. 6. Internal cross-sections of reciprocal systems XIV, XVI, XVIII, XX–XXIII.

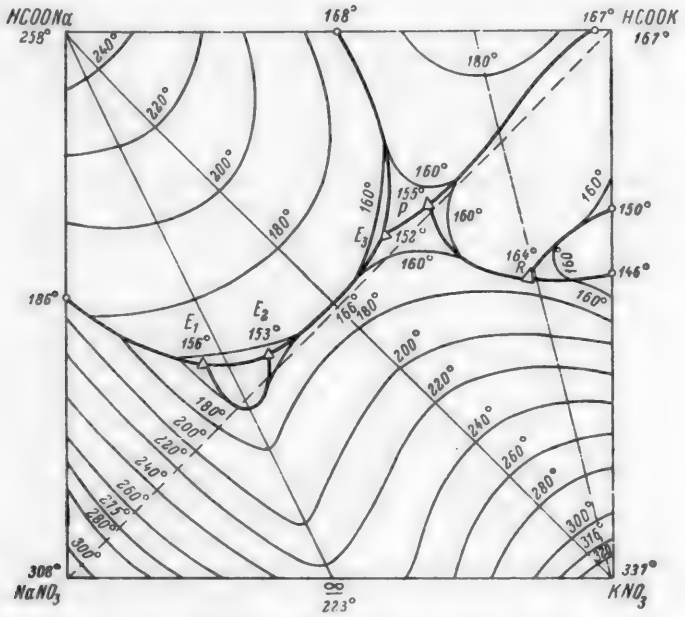

Fig. 7. Projection of the surface of crystallization of the reciprocal system Na, K ‖ NO_3, HCOO on the composition square.

The composition square of the reciprocal system is divided into four phase triangles: 1) $NaNO_3$–$NaNO_3$ · KNO_3–HCOONa, 2) $NaNO_3$ · KNO_3–HCOONa–KNO_3, 3) KNO_3–HCOONa–3HCOOK · HCOONa, 4) 3HCOOK · HCOONa–HCOOK–KNO_3.

A ternary invariant point corresponds to each triangle: E_1, E_2, E_3 and P, the temperatures and compositions of which are shown in Table 3.

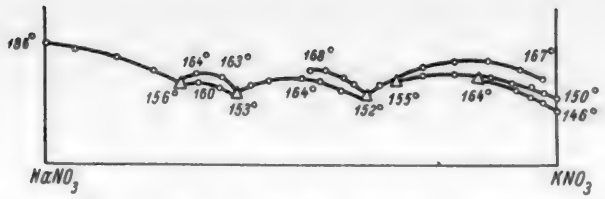

Fig. 8. Projection of the lines of joint crystallization on the $NaNO_3$–KNO_3 side.

TABLE 3

Point	Type	Temp.	Composition (in mole %)			
			HCOONa	HCOOK	KNO_3	$NaNO_3$
E_1	Eutectic	156°	38.5	—	27	34.5
E_2	Eutectic	153	42	—	36.5	21.5
E_3	Eutectic	152	40	23.5	36.5	—
P	Transition	155	35	31.5	33.5	—
R	Transition	164	16	39	45	—

SUMMARY

1. The fusion diagram of the reciprocal system Na, K ‖ NO_3, HCOO was studied.

2. The system is an irreversible-reciprocal system with a stable diagonal. Solid solutions Na, K ‖ NO_3 are stable inside the system down to 165°, while below this temperature they decompose with the formation of compound $NaNO_3 \cdot KNO_3$.

3. A point of double rise is present in the system.

4. Complex-formation in the system does not change the direction of the exchange reaction.

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REDUCTION OF NITROPHENOLS AT A MULTIDROP MERCURY CATHODE

L. N. Vertiulina and N. I. Maliugina

A study of reduction at a dropping-mercury electrode was made by various authors for the purpose of quantitatively determining and establishing the mechanism of the reduction.

Kolthoff and Lingane [1] state that the reduction of aromatic nitro compounds does not go by the scheme proposed by Haber [2], but instead that it proceeds with the addition of 4 electrons to phenylhydroxylamine, in which connection phenylhydroxylamine in acid medium is reduced to aniline, and a second wave is observed on the polarogram. I. A. Korshunov and A. S. Kirillova [3] also came to the same conclusions.

In the early studies on the polarographic reduction of nitrophenols [4] only the reduction potentials of the indicated compounds are given, determined by the method of tangents.

Later Astle and McConnell [5] reduced o-nitrophenol, but the results obtained by them were not confirmed by Stocesova [6], who believes that in neutral medium (pH 6) o-nitrophenol, in contrast to p-nitrophenol, is reduced with the addition of 4 electrons. In either more acid or more alkaline medium the o-nitrophenol is reduced with the addition of 6 electrons. The author explains this by an acid-base catalyzed transformation of o-hydroxyphenylhydroxylamine to the quinone imine, which is then reduced further.

Pearson [7], who studied the reduction of o-, m- and p-nitrophenols in the presence of 8% ethyl alcohol in buffer solutions with pH ranging from 2 to 12, states that in solutions with pH 2 the nitrophenols are reduced with the addition of 6 electrons, while in alkaline medium both o- and p-nitrophenol are also reduced with the addition of 6 electrons, whereas m-nitrophenol is reduced with the addition of only 4 electrons.

Similar results were also obtained by other authors in the presence of 10% ethyl alcohol [8] and in the absence of alcohol [9].

A determination of the composition of the reduction products represents great theoretical and practical interest in the problems dealing with an elucidation of the reduction mechanism of organic compounds. The use of a multidrop mercury cathode for this purpose is convenient, since it permits accumulating the reduction products in amounts sufficient for analysis. In addition, as had been shown by Vodzinskii and Korshunov [10], the electroreduction conditions using a multidrop cathode are quite close to the electroreduction conditions that prevail when the ordinary dropping-mercury cathode is used.

Using the multidrop mercury cathode, we subjected the o-, m- and p-nitrophenols to reduction in acidified aqueous and aqueous-alcohol solutions of sodium sulfate, having a pH ranging from 2 to 2.5, in order to establish the mechanism of their polarographic reduction. Another reason for using aqueous and aqueous-alcohol solutions was to determine the effect exerted by alcohol as a solvent on the reduction of nitrophenols, an effect that has been mentioned by a number of authors [11, 12].

EXPERIMENTAL

We used the apparatus with a multidrop mercury cathode described in [13], which was modified by us slightly in order to make it suitable for our investigations.

In order to compare the results obtained in the electroreduction of nitrophenols in aqueous and in aqueous-alcohol solutions we maintained the electrolysis conditions constant. The electrolysis was run in acidified aqueous and aqueous-alcohol (25% ethyl alcohol by volume) solutions with pH ranging from 2 to 2.5 at 18-20°. The course

of the electrolysis was followed by the value of the limiting current on the polarograms, for which samples were taken at 1-2 hour intervals. At the end of reduction the products were analyzed and the yield of compounds was calculated on the basis of the amount of nitro compound taken for reduction.

The electrolysis was run at a potential slightly higher than the potential of the limiting current, and specifically, for p-nitrophenol at 2.2 v, and for m- and o-nitrophenols at 1.8 v.

During electrolysis the p-nitrophenol solution became dark brown, and a dark brown precipitate deposited. It was found that the electrolyte contains p-aminophenol and p-quinone imine, while the precipitate proved to be p-aminophenol. That p-aminophenol was present in both the electrolyte and precipitate was established by preparing the benzoyl derivative [14]. The melting points of the benzoyl derivatives, and also the mixed melting points of the benzoyl derivatives of the investigated specimens and of pure p-aminophenol, showed quite satisfactory agreement with the literature data, according to which the melting point of the benzoyl derivative of p-aminophenol is 234° [14]. The benzoyl derivatives obtained by us from the precipitate and from the solution, and also their mixtures with the authentic material, had m.p. 230 ± 1°. To quantitatively determine the amount of p-aminophenol in the precipitate and in the electrolyte we used the GOST method [15], based on the reaction of aromatic amines with nitrous acid. p-Quinone imine, formed in small amounts in the electrolysis of p-nitrophenol, did not interfere with the determination of p-aminophenol. The presence of the unstable intermediate product — p-quinone imine — was determined both qualitatively and quantitatively by the amount of iodine liberated, using the method proposed by Bauer [16].

Analysis Results for the Reduction Products of Nitrophenols

Compound	Aqueous solution with pH 2.0			Aqueous-alcohol solution with pH 2.5		
	amount (in %)					
	aminophenol	quinone imine	hydroxyl-amino derivative	amino-phenol	quinone imine	hydroxyl-amino derivative
p-Nitrophenol	82	11	—	48	5	—
o-Nitrophenol	88	4	—	89	5	—
m-Nitrophenol	46	—	48	37	—	37

Analysis of the products of the electroreduction of o-nitrophenol at a multidrop mercury cathode revealed that o-aminophenol and a quinoid derivative of o-nitrophenol are present in the electrolyte. From the electrolyte we isolated the benzoyl derivative of o-aminophenol with m.p. 179 ± 1°, close to the data given in the literature [14] (184°, 182°).

The same as in the case of p-aminophenol, the amount of o-aminophenol was quantitatively determined by the diazotization method. The presence of o-quinone imine was indicated by the red color of the solution, inherent, as is known, to o-quinone derivatives. A quantitative determination of the amount of o-quinone imine was made in the same way as for p-quinone imine.

Qualitative analysis of the reduction products of m-nitrophenol revealed the presence of m-aminophenol and of the hydroxylamino derivative of m-nitrophenol.

The benzoyl derivative of m-aminophenol had m.p. 150°, which is in fairly good agreement with the literature data [14].

We were unable to obtain the benzoyl derivative of the hydroxylamino derivative of m-nitrophenol due to its instability in the presence of atmospheric oxygen.

A quantitative analysis of the reduction products of m-nitrophenol was made by the method described in [17], which method was modified by us slightly in that hydrogen was blown through the silver nitrate solution for 1 hour to remove dissolved oxygen before the silver nitrate solution was mixed with the analyzed solution. It was shown that under the analysis conditions m-aminophenol fails to deposit silver when kept in the dark for a day.

In contrast to the o- and p-nitrophenols, a quinoid compound is not formed in the reduction of m-nitrophenol, since m-quinones do not exist, as is indicated in the literature [18].

The analysis results for the reduction products of the p-, o- and m-nitrophenols in aqueous and aqueous-alcohol solutions at a multidrop mercury cathode are given in the table.

The percent yield of reduction products is the average of several experiments. The determination accuracy of the reduction products was 5-6% (relative).

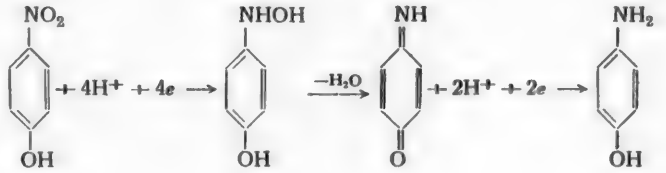
As can be seen from the data in the table, for the p- and m-nitrophenols the yield of reduction products at a multidrop mercury cathode in aqueous-alcohol solutions with pH 2.5 is less than in aqueous solutions.

In the case of o-nitrophenol the yields of reduction products in aqueous-alcohol and aqueous solutions are the same.

DISCUSSION OF RESULTS

The obtained data permit the conclusion that p-nitrophenol is mainly reduced to p-aminophenol, and here p-quinone imine is formed as intermediate product; o-nitrophenol is reduced to o-aminophenol, and in this case the intermediate reduction product is o-quinone imine. The reduction products of m-nitrophenol were the hydroxylamino derivative and m-aminophenol.

The scheme for the reduction of nitrophenols in both aqueous and aqueous-alcohol solutions can be depicted on the example of p-nitrophenol.



The transformations for the ortho and meta isomers can be depicted in similar manner (for the meta isomer without the quinone imine).

In the reduction of the o- and p-nitrophenols the intermediate compounds – the o- and p-quinone imines – are formed in small amounts. Their accumulation in substantial amount does not occur for the reason that they are readily reduced at a multidrop mercury cathode, which is in agreement with the data of the polarographic studies made on compounds having the quinoid bond [1].

m-Aminophenol and the hydroxylamino derivative of m-nitrophenol are formed in nearly equal amounts when m-nitrophenol is reduced at a multidrop mercury cathode under the conditions investigated by us.

The substantial formation of the hydroxylamino derivative of m-nitrophenol can be explained by the fact that its further reduction is evidently made difficult.

It is possible that in this case the potential of the cathode exerts an influence on the reduction rate of the hydroxylamino derivative of m-nitrophenol. A similar influence of the cathode potential on the reduction process was observed by L. I. Antropov and N. T. Vagramian when they studied the reduction of phenylhydroxylamine at a platinum cathode in alcohol-sulfuric acid solutions [19].

The decrease in the yield of products when the p- and m-nitrophenols were reduced in aqueous-alcohol solutions, observed in our investigations, is probably explained by the formation of an intermolecular hydrogen bond, which in aqueous-alcohol solutions is formed with involvement of the alcohol molecule, and this bond, being more stable than the one obtained in aqueous solutions, makes the reduction of the indicated compounds difficult [20].

o-Nitrophenol forms an intramolecular hydrogen bond, which, as is known [1, 20], facilitates reduction of the nitro group in both aqueous and aqueous-alcohol solutions. As a result, a decrease in the yield of reduction products in aqueous-alcohol solutions is not observed in this case.

The authors wish to thank I. A. Korshunov for his valuable advice in the execution of the present work.

SUMMARY

1. As the result of studying the reduction of the o-, m- and p-nitrophenols at a multidrop mercury cathode it was found that nitrophenols in aqueous and aqueous-alcohol solutions with pH from 2 to 2.5 are reduced mainly to o- and p-aminophenols. p- and o-quinone imines, obtained in small amounts, are formed as intermediate products. In the case of m-nitrophenol the reduction products are the hydroxylamino derivative of m-nitrophenol and m-aminophenol, formed in nearly equal amounts.

2. For the p- and m-nitrophenols the yields of reduction products at a multidrop mercury cathode are less in aqueous-alcohol solutions than in aqueous solutions; for o-nitrophenol the yield is the same in both media.

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POLAROGRAPHIC STUDY OF AMINOACETOPHENONES

V. D. Besuglyi, V. N. Dmitrieva and V. V. Dorofeev

Giacometti and Del Marco [1] studied the polarographic behavior of p-acetophenylhydroxylamine and p--aminoacetophenone in buffer solutions with various pH values. The other aminoacetophenone isomers have not been subjected to polarographic study by anybody, although a detailed study of them would permit elucidating the influence exerted by the position of the NH_2 group on the reduction of the carbonyl group in aminoacetophenones.

The reduction of acetophenone and some of its derivatives has been studied in a number of papers [2-8]; here it was established that the reduction of acetophenone proceeds by different mechanisms in acid and in alkaline medium, and that two waves are observed in a certain pH range.

The polarographic behavior of o-, p- and m-aminoacetophenone was studied in the present paper.

EXPERIMENTAL

o-Aminoacetophenone was synthesized by the following scheme [12]

$$C_6H_5CH{=}CHCOOH \xrightarrow{HNO_3} NO_2C_6H_4CH{=}COOH \xrightarrow{Br_2} NO_2C_6H_4(CHBr)_2COOH \xrightarrow{NaOH}$$
$$\longrightarrow NO_2C_6H_4C{\equiv}CCOOH \xrightarrow{t^\circ} NO_2C_6H_4C{\equiv}CH \xrightarrow{H_2} NH_2C_6H_4C{\equiv}CH \longrightarrow NH_2C_6H_4COCH_3$$

The para isomer is formed together with o-aminoacetophenone under the indicated conditions.

The o- and p- isomers were separated during the synthesis: after reducing the nitrophenylacetylene the para isomer crystallized from the mixture of o- and p-aminophenylacetylenes, and this on hydration with dilute sulfuric acid, followed by isolation of the amine, gave p-aminoacetophenone with m.p. 106°. The yield of o--aminoacetophenone was about 8% when calculated on the cinnamic acid. o-Aminoacetophenone was also obtained from o-nitrobenzoic acid through o-nitrobenzoylacetoacetic ester [9].

m-Aminoacetophenone was obtained by the reduction of m-nitroacetophenone with ammonium sulfide, using the Ruppe, Braun and von Zembruski method [10], and was purified by repeated recrystallization from either water or dilute alcohol. The product was obtained as scaly plates with a slight yellow tinge and m.p. 99.2°.

p-Aminoacetophenone was obtained by the acetylation of acetanilide with acetyl chloride [11] in acetic anhydride, followed by hydrolysis of the N-acetyl derivative of p-aminoacetophenone, and then isolation of the p-aminoacetophenone, which was obtained as colorless prisms with m.p. 106°.

The polarographic measurements were made using a FG-8 polarograph with dropping-mercury electrode, the latter having the following characteristics: m = 1.222 mg/sec., t = 2.0 sec., $m^{2/3}t^{1/6} = 1.29\ mg^{2/3}\ sec.^{1/6}$ (E = −1.9 v).

The experiments were run at 18-20°. As a background for the polarography we used: 1) 0.1 N solution of KCl, Li_2SO_4 and $(CH_3)_4NI$; 2) buffer solutions: in the acid region, HCl + KCl; in the region of medium pH values, acetic acid + sodium acetate; in the region of medium and high pH values we also used universal buffer mixtures composed of phenol + phosphoric acid + acetic acid + NaOH. All of the solutions contained from 2 to 8% of C_2H_5OH in water.

In measuring the half-wave potentials a saturated calomel electrode was used as the reference.

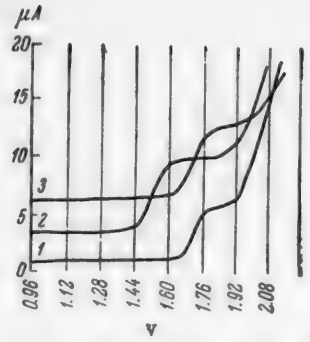

Fig. 1. Polarographic waves of aminoacetophenones (concentration 1.34 mmoles/liter) with a background of 0.1 N Li_2SO_4.
1) o-aminoacetophenone,
2) m-aminoacetophenone,
3) p-aminoacetophenone.

As the results of polarographing with a background of 0.1 N KCl, 0.1 N Li_2SO_4, 0.1 N $(CH_3)_4NI$, etc., showed, all three isomeric aminoacetophenones are reduced at the dropping-mercury electrode. Here for m-aminoacetophenone in the indicated solutions $E_{1/2}$ = −1.53 v, while for the o- and p- isomers the half-wave potentials coincide and are equal to −1.71 v (Fig. 1).

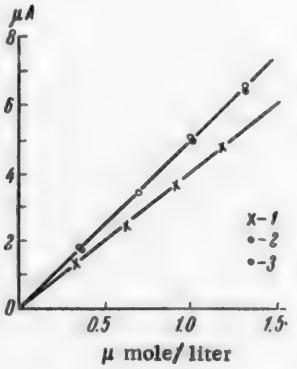

Fig. 2. Linear calibrations of aminoacetophenones with a background of 0.1 N Li_2SO_4.
1) o-aminoacetophenone,
2) m-aminoacetophenone,
3) p-aminoacetophenone.

TABLE 1

Values of the Half-Wave Potentials of o-, m- and p-Aminoacetophenones in Buffer Solutions With Various pH Values

Isomer	pH											
	1.6	2.2	3.72	4.85	5.11	5.74	6.45	6.92	7.54	8.3	9.4	10.7	11.36
o-Aminoacetophenone	−1.04	−1.07	−1.15	−1.24	−1.31	−1.41	−1.46	−1.49,	−1.55,	−1.71		−1.71	
m-Aminoacetophenone	−0.96	−1.00	−1.11			−1.21	−1.38	−1.39,	−1.41,	−1.53	−1.53		−1.53
p-Aminoacetophenone	−0.99	−1.08	−1.16			−1.38	−1.48	−1.50,	−1.56,	−1.71	−1.71		−1.71

The values of the half-wave potentials for all three isomers with a background of buffer solutions with various pH values are shown in Table 1.

The changes in the height of the waves as a function of the pH are shown in Table 2. The linear calibrations of the aminoacetophenones with a background of 0.1 N Li_2SO_4 are shown in Fig. 2.

TABLE 2

Height of the Waves of o-, m- and p-Aminoacetophenone at Various pH Values

Isomer	pH	C (mmole/liter)	Height of wave (mm)		C (mmole/liter)	Height of wave (mm)	
			1st wave	2nd wave		1st wave	2nd wave
o-Aminoacetophenone	1.6	0.99	15		1.34	20.5	
	2.2	0.99	14.5		1.34	19	
	3.72	0.99	13		1.34	18	
	8.3	0.99		11.5	1.34		15.5
	10.7	0.99		11.5	1.34		15.5
m-Aminoacetophenone	1.6	0.67	11		1.34	22	
	2.2	0.67	11		1.34	22	
	3.72	0.67	11		1.34	22	
	5.57	0.67	10.5		1.34	21	
	9.4	0.67		10.5	1.34		21
	11.36	0.67		10.5	1.34		21
p-Aminoacetophenone	1.6	0.67	11.5		1.34	22.5	
	2.2	0.67	11.5		1.34	22.5	
	3.72	0.67	11		1.34	22	
	5.57	0.67	11		1.34	21.5	
	9.4	0.67		11	1.34		21.5
	11.36	0.67		11	1.34		21.5

o-Aminoacetophenone. One well defined polarographic wave is observed in acid medium with a background of buffer solutions with pH ranging from 1.6 to 6.45, and the half-wave potential increases with rise in pH from −1.04 to −1.46 v (Fig. 2). When the polarographing was with a background of 0.1 N solutions of $(CH_3)_4NI$, Li_2SO_4

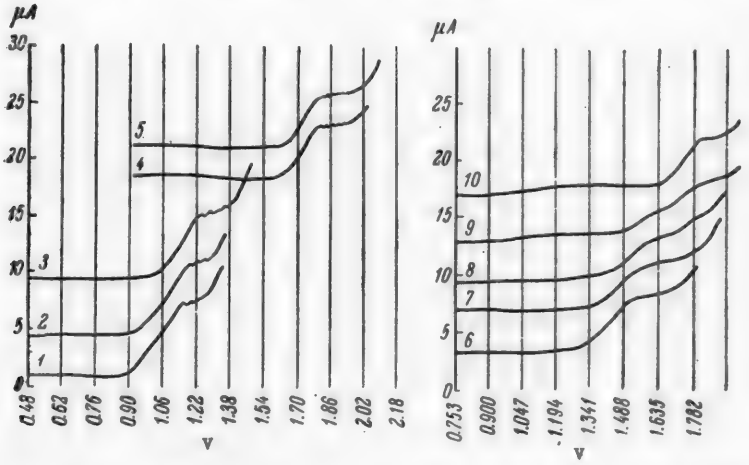

Fig. 3. Polarographic waves of o-aminoacetophenone with a background of buffer mixtures with various pH values. Concentration 1.34 mmoles/liter: 1) pH 1.6, 2) pH 2.2, 3) pH 3.72, 4) pH 8.3, 5) pH 10.7; concentration 1.18 mmoles/liter: 6) pH 5.74, 7) pH 6.45, 8) pH 6.92, 9) pH 7.54, 10) pH 8.00.

and KCl, and also with a background of alkaline buffer solutions with pH > 8, again only one polarographic wave was observed with $E_{1/2}$ = −1.71 v, and the reduction potential did not change with further increase in the pH. This

corresponds to two different polarographic waves. They are observed for o-aminoacetophenone simultaneously in buffer solutions with 6.9< pH< 8; in this connection the potential of the first wave shows a shift when the pH is increased, while the potential of the second wave remains practically constant. Both of these waves are observed simultaneously when o-aminoacetophenone is polarographed with a background of unbuffered acid solutions. By adding a small amount of 0.1 N HCl solution to 0.1 N Li_2SO_4 solution, containing about 1.25 mmoles/liter of o-aminoacetophenone, it becomes possible to follow the rise of the first wave and the disappearance of the second wave (Fig. 4). Thus, for example, when 0.2 ml of 0.1 N HCl solution is added to 10 ml of 0.1 N Li_2SO_4 solution, containing o-aminoacetophenone, besides the second wave (with $E_{1/2}$ = = −1.71 v), there appears a wave with $E_{1/2}$ = −1.17 v. The latter is the first wave that is observed on the polarograms obtained in buffered acid solutions. When 0.3 ml of 0.1 N HCl solution is added the height of this wave increases, while the second wave disappears completely. With further additions of acid the height of the first wave remains unchanged, and still another wave appears, corresponding to hydrogen discharge (the height of this wave is proportional to the concentration of the acid).

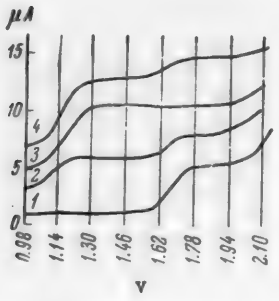

Fig. 4. Polarographic waves of a solution containing 1.25 mmoles/liter of o-aminoacetophenone with a background of 0.1 N Li_2SO_4 (A) with the addition of 0.1 N HCl solution (B).
1) 10 ml A (pH 6.22), 2) 10 ml A + 0.2 ml B (pH 3.28), 3) 10 ml A + 0.4 ml B (pH 3.25), 4) 10 ml A + 0.5 ml B.

The maximum height of the first wave is slightly greater than the sum of the heights of both waves, which in turn is slightly greater than the height of the second wave, obtained in the absence of HCl, as can be seen from the polarograms shown in Fig. 4.

A slight reduction in its height with increase in pH is observed for the first curve with a background of buffered solutions (Table 2). The height of the second wave is independent of the pH.

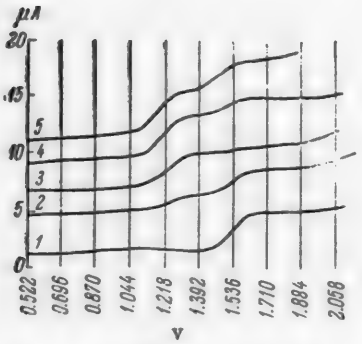

Fig. 5. Polarographic waves of a solution containing 0.67 mmole/liter of m-aminoacetophenone with a background of 0.1 N Li_2SO_4 (A) with the addition of 0.1 N HCl solution (B).
1) 10 ml A, 2) 10 ml A + 0.2 ml B, 3) 10 ml A + 0.4 ml B, 4) 10 ml A + 0.5 ml B, 5) 10 ml A + 0.6 ml B.

<u>m-Aminoacetophenone</u>. One polarographic wave is observed in acid buffer solutions in the pH range of 1.6 to 6.45, and with increase in the pH the half-wave potential shifts from 0.96 v at pH 1.6 to −1.38 v at pH 6.15. A second wave appears in buffer solutions with pH from 6.92 to 7.54, in which connection at pH > 8 the first wave vanishes completely, while the second wave with $E_{1/2}$ = = −1.53 v remains (this value of $E_{1/2}$ does not change with further increase in the pH).

The same as in the case of o-aminoacetophenone, both the first and second waves can be obtained simultaneously by polarographing the meta isomer with a background of unbuffered acid solutions at pH 3-5.5. From Fig. 5 it can be seen that the gradual addition of 0.1 N HCl solution to m-aminoacetophenone with a background of Li_2SO_4 solution leads to the appearance of the first wave, the height of which increases as the pH of the solution decreases. In this connection the height of the second wave decreases in such manner that the sum of the height of the two waves remains constant. The height of the first wave no longer changes after the second wave has disappeared. Further increase in the acidity leads to the appearance of the hydrogen wave.

When m-aminoacetophenone is polarographed with a background of various buffer solutions it can be seen that the height of both the first and second waves is independent of the pH.

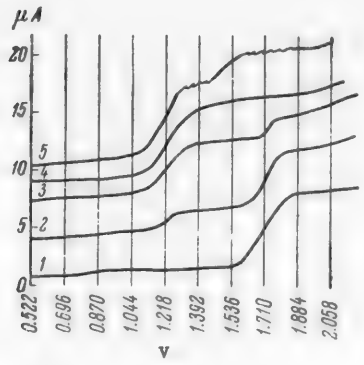

Fig. 6. Polarographic waves of a solution containing 1.34 mmoles/liter of p-aminoacetophenone with a background of 0.1 N Li_2SO_4 (A) with the addition of 0.1 N HCl solution (B).
1) 10 ml A, 2) 10 ml A + 0.1 ml B, 3) 10 ml A + 0.3 ml B, 4) 10 ml A + 0.5 ml B, 5) 10 ml A + 0.7 ml B.

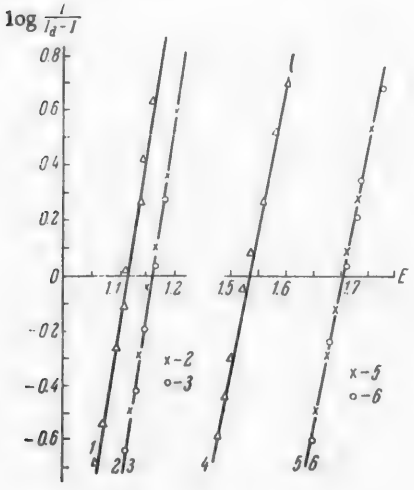

Fig. 7.
Relationship between $\log \frac{I}{I_d - I}$ and E.
1) m-aminoacetophenone, pH 3.37,
2) o-aminoacetophenone, pH 3.37,
3) p-aminoacetophenone, pH 3.37,
4) m-aminoacetophenone, pH 8.3,
5) o-aminoacetophenone, pH 8.3,
6) p-aminoacetophenone, pH 8.3.

p-Aminoacetophenone. The behavior of p-aminoacetophenone at the dropping-mercury electrode almost completely duplicates the behavior of the ortho isomer (Table 1). One wave (the first) is observed with a background of buffer solutions with pH 1.6-6.45. The value of $E_{1/2}$ changes with rise in the pH from −0.99 v at pH 1.6 to −1.48 v at pH 6.45, while a second wave with $E_{1/2}$ = −1.71 v appears in alkaline buffer solutions (pH> 8). Both waves are observed simultaneously for the para isomer in buffer solutions with pH 6.92-7.54; in this connection the height of the second wave at pH 7.54 is lower than in the case of the other two isomers. The first and second waves appear simultaneously with a background of unbuffered acid solutions (Fig. 6). The sum of the heights of both p-aminoacetophenone waves remains constant, and is equal to the height of each of them singly in the absence of the other wave.

The relationships between E and $\log \frac{I}{I_d - I}$ for the investigated isomers are shown in Fig. 7. The slope of the straight lines on this graph shows that in all cases $\alpha < 1$, i.e., the reduction of the aminoacetophenones in both acid and alkaline media is an irreversible process.

Using the Ilkovic equation, we determined the number of electrons involved in the reduction of the aminoacetophenones at the dropping-mercury electrode. For the calculations we took the diffusion coefficient equal to 0.834×10^{-5} sq cm/sec.* Then the following values are obtained for n in the Ilkovic equation: 2.24 for the para, 2.30 for the meta, and 2.18 for o-aminoacetophenone.

The constants of the diffusion current for the investigated isomers in the alkaline region are equal to 3.74 for meta, 3.84 for para, and 2.89 for o-aminoacetophenone. In the acid region they are respectively equal to 3.92, 4.01 and 3.82. For o-aminoacetophenone the slight reduction in the value of the constant of the diffusion current in acid medium is apparently associated with the fact that during storage this isomer showed some tarring, and as a result of this its actual concentration was reduced. This tarring was not observed in the case of the other isomers.

DISCUSSION OF RESULTS

Generalizing the obtained results, it is possible to make the following conclusions. The same as is true with other acetophenone derivatives, the reduction of the aminoacetophenones proceeds by different mechanisms in acid and in alkaline media, in which connection the half-wave potentials have different values in acid and in alkaline

*Obtained by computation from the value of the diffusion coefficient of the benzoate ion in the same medium, equal to 0.881×10^{-5} sq cm/sec, using the formula $\frac{D_1}{D_2} = \frac{\sqrt{M_2}}{\sqrt{M_1}}$ [16].

media. The indicated circumstance leads to the situation that only one wave is observed in buffer solutions with pH < 6.5. With change in the pH of the buffer solution the $E_{1/2}$ shifts by 0.06-0.08 toward negative potentials per pH unit. In buffer solutions with pH > 8 one wave with $E_{1/2} = -1.71$ v is observed in the case of the o- and p-aminoacetophenones, and with $E_{1/2} = -1.53$ v in the case of m-aminoacetophenone.

Two waves are observed simultaneously when the indicated compounds are polarographed in solutions with a pH between 6.5 and 8, the sum of whose heights is approximately equal to the height of the wave in either alkaline or acid medium.

Besides the first wave, a second wave is also observed in unbuffered solutions with pH < 6, corresponding to the wave obtained in buffer solutions with pH > 8.

The appearance of this second wave is associated with a pH change in the layer of solution around the cathode due to consumption of H^+ ions during the reduction of the aminoacetophenone for the reaction corresponding to the first wave. Here the value of the pH in the layer around the cathode shifts toward higher values, and part of the aminoacetophenone molecule is reduced by the mechanism that prevails in an alkaline medium. For this reason the total height of these two waves is approximately equal to the height of the aminoacetophenone wave in the same concentration of solution in either acid or alkaline medium (for the meta and para isomers); for o-aminoacetophenone, as was to be expected from the data given in Table 2, the sum of the heights of the two waves is slightly less than the height of the first wave (appearing in the acid region) and slightly greater than the height of the second wave (Fig. 4).

The scheme for the reduction of the aminoacetophenones can be depicted in the following manner:

in acid medium

$$NH_2C_6H_4COCH_3 + 2H^+ + 2e \longrightarrow NH_2C_6H_4CHOHCH_3, \quad (1)$$

in alkaline medium

$$NH_2C_6H_4COHCH_2 + 2H_2O + 2e \longrightarrow NH_2C_6H_4CHOHCH_3 \quad (2)$$

When the aminoacetophenones are reduced in alkaline medium the hydrogen ions do not take a direct part in the reaction, and consequently the half-wave potential does not depend on the pH.

Since the amino group is an electron-donor group and, being found in either the ortho or para position, increases the electron density in the carbonyl group when compared with the same group in unsubstituted acetophenone, then the reduction of the o- and p-aminoacetophenones in alkaline medium proceeds at more negative potentials than in the case of acetophenone. In the case of m-aminoacetophenone such an electromeric shift of electrons to the CO group is not observed, and consequently the half-wave potential of the meta isomer is close to the $E_{1/2}$ of acetophenone. Holleck and Marsen observed a similar situation when they investigated the reduction of the carbonyl group found in various substituted benzaldehyde derivatives [13].

In acid medium, where the amines are found present as salts, i.e., the nitrogen of the amino group is positively charged (the NH_2 group migrates to NH_3^+ due to the addition of a proton), the tying up of the unshared pair of electrons of the amino group makes it impossible for the p-electrons of this group to couple with the π-electrons of the benzene ring. For this reason all of the aminoacetophenones in acid medium are reduced at potentials lying close to the reduction potential of acetophenone (at pH 2.2, $E_{1/2} = -1.08$ v). A slight divergence in $E_{1/2}$ for the various isomers in acid medium is apparently due only to their variable adsorption at a dropping-mercury cathode.

As regards the differences in the constants of the diffusion current in acid and in alkaline medium, then these differences appear only for the ortho isomer, in which the presence of intramolecular hydrogen-bonding between the CH group and the amino group makes a part of the molecule in alkaline medium incapable of being reduced in the investigated range of potentials. For the other isomers, as had been shown earlier, the constants of the diffusion current are the same in both the alkaline and acid regions.

This explanation of the differences in the behavior of the aminoacetophenones in acid and alkaline media is supported by the spectrographic data obtained by us: on acidification the absorption region of aqueous solutions of the aminoacetophenones shifts toward shorter wavelengths down to the absorption of acetophenone itself. In a

similar manner, aniline in HCl gives the spectrum of benzene, nitroaniline gives the spectrum of nitrobenzene [14], and diphenylamine gives the spectrum of diphenyl [15].

Joint Polarographing of Aminoacetophenones

When m- and p- mixtures, and also m- and o-aminoacetophenone mixtures, are jointly polarographed in either unbuffered neutral media or in alkaline buffer solutions they give two separate waves that are situated quite close to each other – the half-wave potentials differ by 0.18 v for each of the indicated pair of isomers. The joint polarograms for the p- and m-aminoacetophenones are shown in Fig. 8. In acid solutions the waves of the isomers tend to merge, so that the values of $E_{1/2}$ for all three isomers nearly coincide. The total height of the waves of both isomers at pH 6.22 (unbuffered solution), and also at pH 10.7, is slightly less than the sum of the heights of the waves of the isomers, each taken separately, and found in a solution of the same concentration. Both the first and second waves of the ortho and para isomers merge at all pH values of the background. The height of the total wave of the ortho and para isomer is also less than the sum of their heights, each taken separately, and found in the same concentrations.

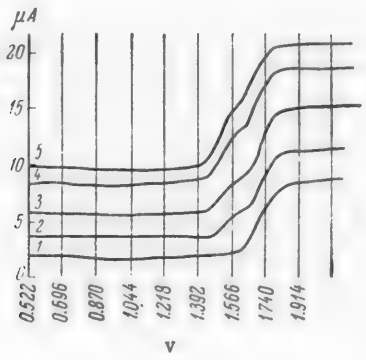

Fig. 8. Polarographic waves of a solution containing 1.34 mmoles/liter of p-aminoacetophenone (A) and various amounts of m-aminoacetophenone (B) in their joint presence with a background of 0.1 N Li_2SO_4.
1) A, 2) A + 0.335 mmoles/liter B, 3) A + 0.670 mmoles/liter B, 4) A + + 1.005 mmoles/liter B, 5) A + 1.340 mmoles/liter B.

As a result, for reasons as yet unknown to us, the isomers when mixed exert a mutual reducing effect on the heights of each other's waves. A similar phenomenon was observed by Adkins and Cox [3]: the height of the acetophenone wave was reduced when benzalacetone was added to the solution, however these authors also failed to give an explanation for the indicated facts.

SUMMARY

1. The characteristics of the polarographic behavior of the o-, m- and p-aminoacetophenones on a dropping-mercury cathode were investigated; here it was shown that they are all reduced in both buffered and unbuffered solutions.

2. The main polarographic constants: $E_{1/2}$, I_d and $\underline{n}$ of the above indicated isomers were determined. It was found that one wave is observed in the acid region (pH < 6.5), the $E_{1/2}$ of which is shifted toward negative potentials with increase in the pH. A second wave is observed in solutions with pH > 8, the $E_{1/2}$ of which remains constant with further change in the pH.

Two polarographic waves are observed for all of the isomers in the pH region 6.5-8.

3. It was shown that the position of the amino group in the aminoacetophenones exerts an influence on their polarographic activity: when in either the ortho or para position the amino group causes the reduction potential of the carbonyl group to shift to the negative side, while when the amino group is in the meta position it is practically without effect on the reduction potential.

4. The possibility of determining the isomeric aminoacetophenones in their joint presence was investigated.

In conclusion we wish to thank A. E. Lutsko for participating in a discussion of the results obtained in this study.

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SYNTHESIS OF VINYL MONOMERS

I. α-SUBSTITUTED DERIVATIVES OF VINYLPHOSPHONIC ACID

A. Ia. Iakubovich, L. Z. Soborovskii, L. I. Muler and V. S. Faermark

The known alkenylphosphonic acid derivatives include α-methylvinylphosphonic acid [1], diethyl α-carbomethoxyvinylphosphonate [2] and diethyl cyanovinylphosphonate [3].

We synthesized a number of derivatives, similar to those indicated above, by the method of oxidative phosphonation [4, 5].

The oxidation of a mixture of methyl acrylate and phosphorus trichloride with oxygen leads to the formation of chlorocarbomethoxyethanephosphonyl dichloride. Of the two isomers possible here, containing either the α--chloro-β-carbomethoxy or the β-chloro-α-carbomethoxy group, it is the latter that is formed. This was shown by converting the mentioned chloride to the diethyl ester, the dehydrochlorination of which with triethylamine gave the diethyl ester of α-carbomethoxyvinylphosphonic acid, identical with the above described [2]. The dimethyl ester of α-carbomethoxyvinylphosphonic acid is obtained in a similar manner. Relative to the properties of these esters it is interesting to mention that their reaction with ammonia under the usual conditions does not lead to the formation of amides.

Attempts to obtain the analogous α-chloro derivative of the vinylphosphonic acid, not reported in the literature, by the Pudovik method [6] from vinylidene chloride and dialkyl phosphite proved unsuccessful. In the presence of catalytic amounts of sodium methylate the reaction fails to go; with an equimolar amount of sodium methylate the formation of a small amount of trimethyl phosphate is observed.

Chlorocyanoethylphosphonic acid derivatives, the dehydrochlorination of which could yield cyanovinylphosphonic acid compounds, were synthesized by the oxidative phosphonation of vinyl cyanide. In this case, in contrast to methyl acrylate, the reaction is accompanied by the formation of two compounds, apparently representing the possible structural isomers of chlorocyanoethanephosphonyl dichloride. However, we were unable to separate these two chlorides by distillation. The separation of the isomers was achieved by converting the mixture of chlorides to the dimethyl esters. One of these esters proved to be a liquid, and the other was crystalline.

The liquid isomer when treated with triethylamine readily cleaves hydrogen chloride, forming the dimethyl ester of cyanovinylphosphonic acid; the position of the cyano group in this compound has not yet been established.

Attempts to synthesize the chlorocyanoethylphosphonic acid derivatives by the addition of phosphorus pentachloride to vinyl cyanide failed to give positive results; even at −15 to −20° the acrylonitrile undergoes chlorination with the formation of dichloropropionitrile.

The previously unknown dimethyl ester of vinylphosphonic acid was synthesized in the usual manner.

The esters of the substituted vinylphosphonic acid form polymers and copolymers with other vinyl monomers.

EXPERIMENTAL

β-Chloro-α-carbomethoxyethanephosphonyl Dichloride (I). Oxygen was passed through a mixture of 17 g of methyl acrylate and 137.5 g of phosphorus trichloride at 0° until reaction was complete. Then the phosphorus oxychloride was removed from the mixture by distillation. The residue was vacuum-distilled. We obtained 67.9 g (69.5%) of (I).

B. p. 124° (8 mm), d^{20}_4 1.5238; $n^{20}D$ 1.4745, MR_D 44.2; calc. 45.25.

Found %: C 20.03, 20.43; H 2.42, 2.51; P 12.93, 13.14. $C_4H_6O_3Cl_3P$. Calculated %: C 20.06; H 2.52; P 12.23.

Dimethyl β-Chloro-α-carbomethoxyethylphosphonate (II). With stirring and a temperature of about 0°, 23.9 g of (I) was gradually added to 100 ml of methanol. After removal of the excess methanol by distillation the residue was vacuum-distilled. We obtained 18 g (79%) of (II).

B.p. 130-132° (7 mm), d^{20}_4 1.3460, $n^{20}D$ 1.4428.

Found %: P 12.88, 13.48. $C_6H_{12}O_5ClP$. Calculated %: P 13.44.

Diethyl β-Chloro-α-carbomethoxyethylphosphonate (III). From 24 g of (I) and 100 ml of absolute ethanol, under the same conditions as described for the preparation of (II), we obtained 20.7 g (80%) of (III).

B.p. 153-155° (8 mm), d^{20}_4 1.2209, $n^{20}D$ 1.4329, MR_D 56.26; calc. 56.56.

Found %: P 11.81, 11.24. $C_8H_{16}O_5ClP$. Calculated %: P 11.90.

Dimethyl α-Carbomethoxyvinylphosphonate (IV). A solution of 23 g of (II) in 100 ml of dry ether was treated with 15.15 g of triethylamine. The next day the obtained precipitate was filtered, washed with ether, and the filtrate was fractionally distilled. We obtained 14.7 g (76%) of (IV).

B.p. 106° (2 mm), d^{20}_4 1.1268, $n^{20}D$ 1.4412, MR_D 40.5; calc. 41.9.

Found %: P 15.95, 15.20. $C_6H_{11}O_5P$. Calculated %: P 15.97.

Diethyl α-Carbomethoxyvinylphosphonate (V). From 25.85 g of (III) and 15.15 g of triethylamine, under the same conditions as described for the preparation of (IV), we obtained 16.5 g (75%) of (V).

B.p. 118-119° (3 mm), d^{20}_4 1.1621, $n^{20}D$ 1.4348, MR_D 49.8; calc. 51.2.

Found %: P 12.72, 12.91. $C_8H_{15}O_5P$. Calculated %: P 13.09.

Cyanochloroethanephosphonyl Dichloride (VI). Oxygen was passed through a mixture of 53 g of acrylonitrile and 344 g of phosphorus trichloride at 10-20° until reaction ceased. The formed phosphorus oxychloride was removed from the reaction mixture at 50° (50-60 mm). The residue was distilled at 2 mm. The following fractions were isolated: 1st, 50-95° (9 g), 2nd, 95-105° (60 g), and 3rd, residue (20 g).

Redistillation of the 2nd fraction gave 33.6 g (16.6%) of (VI).

B. p. 99-101° (2 mm), d^{20}_4 1.5721, $n^{20}D$ 1.4783, MR_D 38.5; calc. 38.8.

Found %: C 17.05, 17.21; H 2.22, 1.89; Cl (hydrolyzable) 34.28; N 6.67, 6.69; P 14.63, 15.26. $C_3H_3OCl_3NP$. Calculated %: C 17.43; H 1.44; Cl (hydrolyzable) 34.88; N 6.77; P 15.00.

Dimethyl Cyanochloroethylphosphonate (VII). With stirring and a temperature of about 0°, 30 g of (VI) was gradually added to 140 ml of methanol. The excess methanol was removed in vacuo. The residue, an only liquid mixed with crystals, was treated with dry ether. Here the oily liquid went into solution. After separation from the crystals, the solution was fractionally distilled. After 2 fractional distillations we obtained 5.8 g of (VII).

B. p. 134-135° (2 mm), d^{20}_4 1.3275, $n^{20}D$ 1.4403, MR_D 39.3; calc. 40.7.

Found %: C 31.2, 30.9; H 4.20, 3.80; Cl 17.68; 17.35; N 6.48, 6.24; P 15.44, 15.61. $C_5H_9O_3ClNP$. Calculated %: C 30.38; H 4.55; Cl 17.97; N 7.08; P 15.69.

The product is insoluble in water. The water extract does not give a test for chloride ion.

Treatment of the ether solution of the product with triethylamine gave a precipitate of triethylamine hydrochloride.

Dimethyl Cyanovinylphosphonate (VIII). From 8 g of (VII) and 8 g of triethylamine, under the same conditions as described for the preparation of (IV), we obtained 1.8 g of (VIII).

B. p. 95-96° (2 mm),* d^{20}_4 1.2458, $n^{20}D$ 1.4327.

*From the amount of chlorine which was contained in the triethylamine hydrochloride precipitate it could be assumed that the dehydrochlorination had gone to the extent of 80%. However, considerable decomposition of the product occurred during distillation.

Found %: N 8.61, 8.92; P 18.98, 19.17. $C_5H_{13}O_3NP$. Calculated %: N 8.7; P 19.25.

Dimethyl Vinylphosphonate (IX). A solution of 18.5 g of potassium hydroxide in 120 ml of methanol was added in drops to 45 g of dimethyl β-chloroethylphosphonate. The mixture was heated on the water bath for one hour, and then allowed to stand overnight. The obtained precipitate of potassium chloride was filtered and washed with methanol. The methanol was distilled from the filtrate, and 36 g (80%) of (IX) was obtained from the residue.

B. p. 82-84° (3.5 mm), d^{20}_4 1.1696, $n^{20}D$ 1.4305, MR_D 30.58; calc. 31.17.

Found %: P 22.40, 22.27. $C_4H_9O_3P$. Calculated %: P 22.8.

SUMMARY

1. The oxidative phosphonation of methyl acrylate and acrylonitrile gave the corresponding chlorocarbomethoxy- and chlorocyanoethanephosphonyl dichlorides, and these treated with alcohols gave the corresponding esters.

2. Dehydrochlorination of the above mentioned esters led to obtaining cyano- and carboalkoxy-substituted vinylphosphonates.

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*Original Russian pagination. See C. B. Translation.

SYNTHESIS OF VINYL MONOMERS

II. SOME DERIVATIVES OF α-CHLOROACRYLIC ACID

A. Ia. Iakubovich, E. P. Pravova and N. A. Bogoslovskii

Many derivatives of α-chloroacrylic acid as yet remain unknown. The synthesis of some of these compounds is described below.

The previously unknown α-chloroacryloyl fluoride was obtained by us from the corresponding acid halides. The method of A. N. Nesmeianov and E. Kan [1] was used to obtain the indicated fluoride in 45% yield. Attempts to synthesize the fluoride by heating (160-170°) α-chloroacrylic acid with benzoyl fluoride or by the exchange reaction of α-chloroacryloyl chloride with potassium fluoride gave negative results. The α-chloroacryloyl chloride was obtained by us not by the dehydrochlorination of dichloropropionyl chloride [2], but instead directly from α-chloroacrylic acid. The best yield (40%) was obtained when the acid was reacted with benzoyl chloride; the yields of α-chloroacryloyl chloride were lower when other acid chlorides (PCl_3, $SOCl_2$, $C_6H_5CCl_3$) were used.

Using the α-chloroacryloyl chloride, we synthesized by conventional procedures the p-cyclohexylphenyl ester (new), N-phenylamide (new) and ethyl ester of α-chloroacrylic acid. In its properties the ethyl α-chloroacrylate failed to differ from the previously described ester [2-4], and was obtained by us by the direct esterification of α-chloroacrylic acid with ethanol. The mentioned α-chloroacrylic acid derivatives are capable of giving polymers and copolymers with vinyl monomers.

EXPERIMENTAL

α-Chloroacryloyl Fluoride (I). A mixture of 128 g of benzoyl chloride, 58 g of fused potassium fluoride powder and about 30 g of α-chloroacrylic acid was charged into a round-bottomed flask, fitted with thermometer, a Vigreux column with a height of 10-15 cm, condenser, and a receiver, cooled in ice and protected by a calcium chloride tube. The mixture was heated to 80-90°, where a stormy reaction began, and (I) began to distill; another 23 g of α-chloroacrylic acid was added in portions (4-5 g) when the distillation began to slow up. At the end the bath temperature was raised to 150°, and the distillate up to 130° collected. Redistillation of the distillate gave 27 g of (I) with b.p. 67-67.5°. Yield 45%. The substance is a clear, colorless liquid that fumes in the air, and whose vapors irritate the mucous membranes; the substance etches glass when stored in it.

Found %: Cl 31.5; F 16.8. C_3H_2OClF. Calculated %: Cl 32.7; F 17.51.

α-Chloroacryloyl Chloride (II). a) A mixture of 205 g of benzoyl chloride, 78 g of α-chloroacrylic acid, 5.66 g of cuprous chloride and 2.83 g of hydroquinone was charged into a Claisen flask, fitted with a descending condenser and receiver. Vacuum was applied to the system (residual pressure 76 mm), and the flask contents were gradually heated on the water bath to 80°. The acid chloride formed here was distilled off (vapor temperature 45-69°). The yield of crude acid chloride obtained in this manner was 48.5 g. Redistillation gave 35.5 g (39%) of (II) as a clear, colorless liquid that fumed in the air and had a very sharp lachrymatory odor. B. p. 46-47° (76 mm), $n^{20}D$ 1.4720, d^{20}_{20} 1.3628.

b) A mixture of 5 g of α-chloroacrylic acid, 9.2 g of benzotrichloride, 0.47 g of cuprous chloride and 0.2 g of fused zinc chloride was heated in a flask under reflux at 70-75°. Heating was continued until hydrogen chloride ceased to evolve. Vacuum-distillation of the reaction mixture gave 1.6 g of (II) with b.p. 46-47° (76 mm). Yield 27%.

c) A solution of α-chloroacrylic acid in methanol was neutralized with the calculated amount of a 10 % sodium methylate solution in methanol. Here the sodium salt separated as a white crystalline precipitate; the remainder of the salt was obtained when the solution was evaporated in vacuo. A mixture of 5 g of sodium α-chloroacrylate, 9.26 g of thionyl chloride and 0.22 g of cuprous chloride was heated at 70-80° for 45 minutes. The excess thionyl chloride was distilled off and the residue was vacuum-distilled. We obtained 1.7 g (38%) of (II) with b.p. 46.5-47° (76 mm).

N-Chloroacrylanilide (III). A 10% solution of 1.5 g of aniline in benzene was added to a 10% benzene solution of 1 g of (II). In 10-15 minutes the precipitate of aniline hydrochloride was filtered, and the filtrate was evaporated in vacuo. The residue (1.2 g) was recrystallized from aqueous alcohol to give 1 g of pure (III) as colorless crystals (m.p. 52.5-53.5°), insoluble in water, and readily soluble in the common organic solvents.

Found %: C 59.9; H 4.26; N 7.23. C_9H_8ONCl. Calculated %: C 59.5; H 4.4; N 7.71.

p-Cyclohexylphenyl α-Chloroacrylate (IV). The starting p-cyclohexylphenol was synthesized by the Meyer and Bernhauer method [5]. We obtained a melting point of 122-123° (instead of the indicated 131-132°). The yield was several percent of the theoretical (based on cyclohexanol).

A suspension of 3 g of dry sodium p-cyclohexylphenate in 20 ml of benzene was treated with a solution of 2.4 g of (II) in 10 ml of benzene. The reaction mixture was heated at 75° for 1.5 hours, cooled, and filtered. Evaporation of the filtrate gave 3.1 g of residue. After 2 recrystallizations of the residue from alcohol, and then from petroleum ether, we obtained 0.8 g of pure (IV) as colorless crystals with m.p. 62.5-63.5°. The substance is readily soluble in organic solvents, and insoluble in water. Yield 20%.

Found %: C 67.29; H 6.96; Cl 11.63. $C_{15}H_{17}O_2Cl$. Calculated %: C 68.0; H 6.45; Cl 13.5.

Ethyl α-Chloroacrylate (V). a) To 35.6 g of absolute ethyl alcohol was added in drops 21 g of (II) at 50-55°, after which the mixture was heated at 100° until HCl was no longer evolved, and then it was vacuum-distilled, having added antioxidant (N-phenyl-2-naphthylamine). We obtained 6-6.5 g of (V) with b.p. 52.5-53.5° (18 mm), $n^{20}D$ 1.4384.

b) A mixture of 10.7 g of α-chloroacrylic acid, 9.2 g of absolute ethyl alcohol and 0.8 ml of concentrated sulfuric acid was heated under reflux for 3 hours, then the mixture was neutralized with soda, filtered, and vacuum-distilled. We obtained 3.6 g of (V) with b.p. 43-45° (15 mm), $n^{20}D$ 1.4384.

SUMMARY

The syntheses of the acid fluoride, the acid chloride and some of the previously unknown derivatives of α-chloroacrylic acid were described.

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DECARBOXYLATION OF ACRIDINE-9-CARBOXYLIC ACIDS WITH CARBONYL-CONTAINING COMPOUNDS

A. I. Gurevich

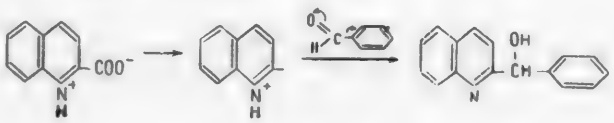
Secondary reactions accompanying the decarboxylation of heterocyclic carboxylic acids in a solvent have been little studied. Dyson and Hammick [1] observed that quinaldinic and isoquinaldinic acids dissolved in aromatic aldehydes and ketones form the corresponding carbinols or ketones on decarboxylation as a result of condensation. In later reports by Hammick and coworkers [2-6] and Mislow [7] the range of the reaction was extended. It was established that picolinic, isonicotinic, and cinchoninic acids undergo analogous transformations and that the second component in the condensation may be quinoline, dinitrobenzene, dinitrochlorobenzene, or an ester of an aromatic or aliphatic-aromatic acid. It was also established that the decarboxylation of quinaldinic [5] and picolinic [8] acids is a first-order reaction. It was suggested that the acids being decarboxylated exist in the form of zwitter-ions, and that the carbanion formed on decarboxylation reacts like the CN ion.

In the present report analogous reactions of acridine-9-carboxylic acid are studied. The acids were decarboxylated in various aldehydes and ketones and in ethyl p-nitrobenzoate at a temperature of the order of 200° in a nitrogen stream (in order to avert oxidation of possible reaction products by atmospheric oxygen).

As a result of the reaction of acridine-9 carboxylic acids with the appropriate aldehydes we obtained 9-benzoyl-, 9-o-chlorobenzoyl-, and 9-p-nitrobenzoylacridines, as well as 2-methoxy-6-chloro-9-(p-nitrobenzoyl)acridine. The yield was about 30% in all cases. The synthesized substances do not form the usual ketone derivatives (phenylhydrazones, thiosemicarbazones), and the presence of the ketone function in these compounds is assumed on the basis of the absence of active hydrogen atoms.

We attempted to carry out the analogous reactions of acridine-9-carboxylic acid with benzophenone and p-nitroacetophenone, as well as those of 2-methoxy-6-chloroacridine-9-carboxylic acid with 1-diethylaminopentanone-4 and ethyl p-nitrobenzoate. In all cases only the corresponding acridines, unsubstituted in position 9, were isolated; yields were 44, 87, 64 and 18%, respectively. Condensation with ketones and carboxylic acid esters, unlike analogous reactions in the pyridine and quinoline series, is probably impossible owing to the steric inaccessibility of the carbonyl carbon atom to the acridine radical.

We noticed that while decarboxylation of 2-methoxy-6-chloroacridine-9-carboxylic acid in the solvent p-nitrobenzaldehyde proceeds relatively slowly even at a temperature of the order of 200°, decarboxylation in the solvents p-dimethylaminobenzaldehyde and 1-diethylaminopentanone-4 goes rapidly even at 80-100°. This undoubtedly contradicts the assertion of Hammick et al. [5] that the activation energy of the decarboxylation reaction does not depend on the solvent. In the last two cases an ionic reaction mechanism should undoubtedly be assumed. However, we were unable to isolate the product of condensation with p-dimethylaminobenzaldehyde (only 2-methoxy-6-chloroacridine was isolated, with a yield of 66%), which creates doubt as to the correctness of the scheme with an ionic reaction mechanism, proposed by Brown and Hammick [4].



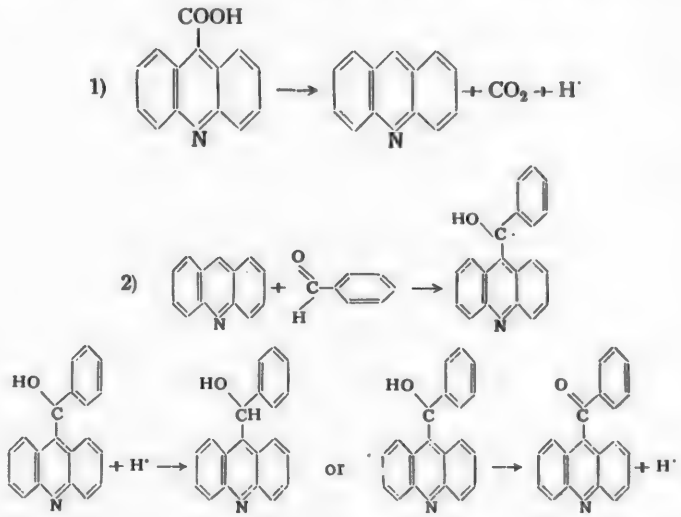
The fact that in our experiments substituents in the ring of the aldehyde were found to have no substantial

effect on the yield of the condensation product also fails to conform to this scheme.

Furthermore, the Brown-Hammick scheme does not explain the fact that in a number of cases the reaction products are not carbinols but ketones. It does not seem very likely that these carbinols could easily be oxidized in an aldehyde medium and a nitrogen atmosphere.

We attempted to synthesize such carbinols in the acridine series since in our decarboxylation experiments we always obtained only ketones, and, according to Brown [6], it was to be expected that these carbinols would be very easily oxidized in air to the corresponding ketones. We were unable to reduce either 9-(o-chlorobenzoyl)acridine or 9-(p-nitrobenzoyl)acridine by prolonged heating at 80° with aluminum isopropoxide in isopropyl alcohol. We hydrogenated 9-benzoylacridine in alcohol over Raney nickel. On oxidation of the (9,10-dihydroacridyl-9)--phenylcarbinol thus obtained with ferric chloride in hydrochloric acid solution, acridine was isolated with an 80% yield. Oxidation of the dihydroacridylphenylcarbinol by air led to (acridyl-9)-phenylcarbinol but not to 9--benzoylacridine, which would necessarily have resulted if (acridyl-9)-phenylcarbinol had been easily oxidized by air.

The noted facts may be explained by assuming that decarboxylation accompanied by condensation of the heterocyclic radical with the solvent is accomplished by the radical mechanism



In conclusion I express my thanks to A. M. Grigorovskii for his valuable advice, which made possible the completion of the present work.

EXPERIMENTAL

9-Benzoylacridine (I). A mixture of 2 g of acridine-9-carboxylic acid (II) and 50 ml of benzaldehyde was refluxed 5 hours at 160-165° in a nitrogen stream. Excess benzaldehyde was distilled in vacuo from the homogeneous mixture obtained. The residue was diluted with 50 ml of ether. The ether evaporated on long standing, and after this the residue contained a crystalline substance. The crystals were filtered, washed with ether, and dried in a vacuum-desiccator. The yield of (I) was 0.8 g (29.6%). M.p. 216-217° after recrystallization from alcohol [9, 10].

Found %: C 80.25, 80.40; H 4.76, 4.77; N 4.74; H_2O 4.50. $C_{20}H_{13}ON \cdot H_2O$. Calculated %: C 79.73; H 4.98; N 4.65; H_2O 5.98.

Hydrochloride: m.p. 228-234° (from 2 N hydrochloric acid).

Found %: Cl 11.00. $C_{20}H_{14}ONCl$. Calculated %: Cl 11.11.

9-(o-Chlorobenzoyl)acridine (III). A mixture of 7 g of (II) and 44 g of o-chlorobenzaldehyde was refluxed 5 hours at 175-185° in a nitrogen stream. Excess o-chlorobenzaldehyde was distilled in vacuo from the homoge-

neous mixture obtained. The residue was diluted with 300 ml of ether. Without removing the slight suspended precipitate the ethereal solution was saturated with hydrogen chloride. The precipitated hydrochloride mixture was filtered, washed with ether, and dried in a vacuum-desiccator. The dried hydrochloride mixture was heated to boiling with 300 ml of water acidified with 0.5 ml of concentrated hydrochloric acid, 7 g of sodium sulfite was added, the mixture was boiled 5 minutes, and the hot solution was filtered and made alkaline with caustic soda. The yield was 1.85-2.00 g of acridine (32.9-35.6%) with a m.p. of 105-107°. The residue which did not dissolve in water on treatment of the hydrochlorides with sodium sulfite was twice recrystallized from 70% acetone; (III) was obtained. The aqueous-acetone mother liquor was concentrated, and the precipitated (III) was again recrystallized. Total yield, 2.6-2.9 g (26.0-29.0%). M.p. 182-183°.

Found %: C 75.09; H 3.89; N 4.65, 4.75; Cl 10.87, 11.16. $C_{20}H_{12}ONCl$. Calculated %: C 75.59; H 3.78; N 4.41; Cl 11.18.

Hydrochloride: m.p. 255-256° (from 2 N hydrochloric acid).

9-(p-Nitrobenzoyl)acridine (IV). A mixture of 2 g of (II) and 11.5 g of p-nitrobenzaldehyde was refluxed one hour at 170-190° in a nitrogen stream. The reaction mixture was then treated by boiling with 750 ml of 2 N hydrochloric acid, and the solution was separated from the oil. The precipitate which settled out of the solution on cooling was filtered and washed with acetone. The yield of hydrochloride (IV) was 0.7 g (21.4%). The hydrochloride was dissolved in a mixture of acetone and a few drops of concentrated ammonia, and the solution was filtered and diluted with water. (IV) was obtained; m.p. 219-221° [11].

Found %: C 69.91, 70.07; H 4.05, 4.00; N 8.36, 8.49; H_2O 4.48. $C_{20}H_{12}O_3N_2 \cdot H_2O$. Calculated %: C 69.37; H 4.04; N 8.09; H_2O 5.20.

2-Methoxy-6-chloro-9-(p-nitrobenzoyl)acridine (V). A mixture of 3 g of 2-methoxy-6-chloroacridine-9-carboxylic acid (VI) and 15 g of p-nitrobenzaldehyde was refluxed 1.5 hours at 190-200° in a nitrogen stream. The reaction mixture was then dissolved in acetone; the solution was diluted with water. The precipitate which settled out was filtered and treated by boiling with 300 ml of 2 N hydrochloric acid, the solution was filtered and neutralized with ammonia, and the precipitate was filtered and washed with water. The residue undissolved in hydrochloric acid was again dissolved in acetone, diluted with water, and worked up like the preceding. After repeated treatment 1.3 g of (V) was isolated; m.p. 236-238° after reprecipitation from acetone by water.

Found %: C 64.61, 64.38; H 3.74, 3.48; N 7.70, 7.89; Cl 8.88, 8.70. $C_{21}H_{13}O_4N_2Cl$. Calculated %: C 64.20; H 3.31; N 7.14; Cl 9.04.

Decarboxylation of (VI) in p-dimethylaminobenzaldehyde. A mixture of 5 g of (VI) and 20 g of p-dimethylaminobenzaldehyde was refluxed at 200° in a nitrogen stream. At 100° vigorous decarboxylation had already begun; after 15 minutes the mixture became homogeneous and CO_2 evolution ceased. Excess p-dimethylaminobenzaldehyde was distilled off in vacuo. The residue was dissolved by boiling with 750 ml of 0.2 N hydrochloric acid, the solution was filtered, and to it was added 75 ml of concentrated hydrochloric acid; the precipitate which settled out on cooling consisted of 2-methoxy-6-chloroacridine hydrochloride. Yield, 2.8 g (66.1%); m.p. 243-245°. 2-Methoxy-6-chloroacridine was precipitated from an aqueous solution of the hydrochloride with ammonia and recrystallized from aqueous acetone. M.p. 181-182° [12].

Found %: C 69.27, 69.23; H 4.50, 4.40; N 5.33; Cl 14.13. $C_{14}H_{10}ONCl$. Calculated %: C 69.54; H 4.11; N 5.75; Cl 14.61.

(9,10-Dihydroacridyl-9)phenylcarbinol (VII). Hydrogenation of 0.5 g of (I) in 60 ml of alcohol was accomplished over 0.5 g of Raney Ni in the course of 5 hours at 50°; the mixture was cooled and filtered, the filtrate concentrated in vacuo to 20 ml, and the residue diluted with water. The precipitate which separated out was filtered and dried in a vacuum-desiccator. The yield of (VII) was 0.32 g; m.p. 204-205° after recrystallization from alcohol.

Found %: C 83.58; 83.42; H 6.24, 6.17; N 4.75, 5.13. $H_{act.}$ 1.16, 1.35. $C_{20}H_{17}ON$.
Calculated %: C 83.62; H 5.92; N 4.88; $H_{act.}$ 0.70.

(Acridyl-9)phenylcarbinol (VIII). Air was blown through a solution of 0.1 g of (VII) in 40 ml of alcohol at 50° for 5 hours. The alcohol was evaporated in vacuo, and 0.09 g of (VIII) was obtained; m.p. 189-191° after recrystallization from alcohol. Melting point of a sample mixed with (VII), 182-185°. Melting point of a sample

mixed with (I), 180-185°.

Found %: $H_{act.}$ 0.40. $C_{20}H_{15}ON$. Calculated %: $H_{act.}$ 0.35.

SUMMARY

1. The decarboxylation of acridine-9-carboxylic acids dissolved in carbonyl-containing compounds has been studied. It has been shown that 9-benzoylacrdine derivatives are formed by secondary reaction with the aldehydes. In ketones and carboxylic-acid esters secondary reactions are not observed, probably owing to steric hindrance.

2. The ionic reaction mechanism proposed earlier does not explain certain discovered facts.

3. A scheme with a radical reaction mechanism is proposed.

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ON THE PRODUCTS FORMED IN THE CONDENSATION OF n-BUTANOL IN THE PRESENCE OF SODIUM BUTOXIDE AND A COPPER CATALYST

V. I. Liubomilov and E. T. Belianina

In the production of 2-ethylhexanol by the condensation of n-butanol in the presence of sodium butoxide and a dehydrogenating catalyst [1], the hydrogen evolved in the reaction has the odor of butyraldehyde. This aldehyde was proved by preparing the 2,4-dinitrophenylhydrazone. Further, on separation of the reaction products it was found that the 180-185° fraction corresponding to 2-ethylhexanol-1 contains an unsaturated compound which is characterized by its bromine number. From this fraction we isolated the unsaturated alcohol 2-ethylhexenol-1, identical to the unsaturated alcohol obtained by Braun and Manz [2] by dehydration of octylene glycol [octoglycol] ether. To this alcohol they ascribe the structure of α-ethyl-β-n-propylallyl alcohol. Acid products were isolated from the sodium salts formed in the condensation of n-butanol and were studied. Besides butyric and 2-ethylcaproic acids [3], the lactone $C_{12}H_{22}O_2$ was also isolated.

EXPERIMENTAL

Condensation of n-butanol. A flask with a stirrer, reflux condenser, and thermometer was charged with 300 g of n-butanol, and 32 g of metallic sodium was dissolved in the latter. The flask was heated in an oil bath to 125-130°, and into it was put 0.6 g of basic copper carbonate catalyst* previously dried in an oven at 120-130°. Evolution of hydrogen began in 20-30 minutes. The reaction was continued for 10-12 hours, until hydrogen evolution had almost entirely ceased. The reaction product was steam distilled. The residue in the flask, which consisted of an aqueous solution of sodium salts, was filtered to remove the catalyst, concentrated by evaporation, and acidified with 42 ml of 90% sulfuric acid. The organic acids separated out in the form of an oily layer.

Yields and Properties of Products Isolated from Salts

Products	Yield (in g)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Acid number	
					found	calculated
Butyric acids	412.7	161—162° (737), 105—108 (80)	0.9585	1.3992	633	637
2-Ethylcaproic acid	128.6	227—228 (750), 113—114 (7.5)	0.9118	1.4274	384	389
Lactone*	71.7	132—134 (7.5)	0.9642	1.4622	0	0

*The properties are given for a product washed in soda solution and water, and redistilled.

Proof of the presence of butyraldehyde. The hydrogen was passed through a bottle containing a saturated alcoholic solution of 2,4-dinitrophenylhydrazine. The 2,4-dinitrophenylhydrazone was obtained in the form of long, yellow needles, m.p. 121.5-122° (from alcohol). Literature data [4]: m.p. 122-123°.

*The authors express their cordial thanks to B. M. Dubinin, who recommended the use of this catalyst.

2-Ethylhexenol-1. The steam-distilled products were separated from the water and rectified. After repeated rectification of the intermediate fractions there were obtained: 38.0 g of n-butanol, 103.5 g of the 180-185° fraction, and 13.5 g of still residue. The bromine number of the 180-185° fraction was 32.5. From a series of experiments conducted under similar conditions several kilograms of the 180-185° fraction was obtained. By means of a series of successive rectifications of the latter in vacuo with a column having an efficiency of about 20 theoretical plates, we were able to obtain a small quantity of a substance, the properties of which did not change on subsequent rectification:

b.p. 177.5-178.5° (760 mm), b.p. 60° (9 mm), d^{20}_4 0.8427, $n^{20}D$ 1.4428.

Found %: OH 13.6. Bromine number 1254, 1248. $C_8H_{15}OH$. Calculated %: OH 13.3. Bromine number 1248.

Literature data [2]: b.p. 68-71°(12 mm), d^{22}_4 0.8414, $n^{22}D$ 1.4418.

2-Ethylhexanol-1 was obtained in pure form by hydrogenation of the 180-185° fraction or by treatment of the latter with an aqueous potassium permanganate solution, steam distillation, and rectification:

b.p. 183-184°, d^{20}_4 0.8325, $n^{20}D$ 1.4325; bromine number 0.

Note that on careful rectification of the 180-185° fraction the end fractions had higher bromine numbers than the middle ones. This indicated the possible presence of a second isomer of 2-ethylhexenol-1.

Investigation of acid products. The 700-g quantity of acid products accumulated from a series of experiments was rectified in vacuo. The yields and properties of the fractions obtained are given in the table.

The fraction with an acid number of 0 was a colorless liquid, more viscous than the preceding fractions, insoluble in water, and soluble in organic solvents. On treatment of this fraction by slight heating with 2% aqueous alkali it gradually dissolved, but on acidification with sulfuric acid it separated out unchanged.

Found %: C 71.80; H 11.24. Ester number 271. $C_{12}H_{22}O_2$. Calculated %: C 72.67; H 11.19. Ester number 282.

SUMMARY

In the condensationof n-butanol in the presence of sodium butoxide, besides 2-ethylhexanol-1, 2-ethylhexenol-1 is formed. Besides butyric and 2-ethylcaproic acids, the lactone $C_{12}H_{22}O_2$ was isolated from the carboxylic acid salts.

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REACTION OF BUTYRALDEHYDE WITH A SOLUTION OF SODIUM BUTOXIDE IN n-BUTANOL

V. I. Liubomilov

The condensation of n-butanol in the presence of its sodium alcoholate and a catalyst [1] leads to the formation, together with 2-ethylhexanol-1, of the corresponding unsaturated alcohol. In connection with the preceding reports [2, 3] it was of interest to make sure of the formation of the stated alcohols in the reaction of butyraldehyde with a solution of sodium butoxide in n-butanol. They were indeed prepared and isolated in this reaction. In the fraction corresponding to a mixture of 2-ethylhexanol-1 with unsaturated alcohols there are probably two isomers of 2-ethylhexenol-1, one of which was isolated in pure form and proved to be identical with the alcohol isolated from the product of n-butanol condensation [1]. Of the properties of this isomer, its ability to isomerize to 2-ethylhexanal-1 on passing over an incandescent silver wire should be noted.

EXPERIMENTAL

Reaction of butyraldehyde with a solution of sodium butoxide in n-butanol. A flask with a stirrer, reflux condenser, thermometer, and dropping funnel was charged with a weighed portion of n-butanol, and a weighed portion of metallic sodium was dissolved in the latter. The flask was heated in an oil bath, and a weighed portion of butyraldehyde was trickled into it from a dropping funnel during a fixed time interval. Then the flask was cooled, the reaction product steam-distilled, the distilled alcohols redistilled with a herringbone fractionating column 20 cm high, and the fraction with the boiling range 175-182° was separated out. The results of the experiments are given in the table.

Condensation of Butyraldehyde with a Solution of Sodium Butoxide in n-Butanol

Charge (in g)			temp.	Addition time of aldehyde (in hours)	Yield of 175 -182° fraction (in g)	Bromine numbers of 175-182° fraction
n-butanol	sodium	butyraldehyde				
80	8	26	70°	0.5	0	—
80	8	26	100	0.5	4.1	792
80	8	26	110	0.5	9.72	876
80	8	26	130	0.5	14.15	804
80	9.9	26	140	0.5	14.05	852
80	9.9	26	110	0.5	10.8	845
80	4.0	26	110	0.5	3.45	788
80	8	19.4	130	0.5	9.50	818
80	8	38.8	130	1.0	12.1	777
320	32	104	130	2.5	54.5	729
1600	160	520	130	6.0	344.2	513
80	8	26	130	5.0	14.5	615

First isomer of 2-ethylhexenol-1. On slow rectification of the 175-182° fraction in vacuo with a column of about 20 theoretical plates, fractions with high bromine numbers (over 1000) were obtained. Repeated rectification permitted the isolation of a substance with the following properties:

b.p. 177-178° (755 mm), b.p. 70-71° (12 mm), d^{20}_4 0.8418, $n^{20}D$ 1.4438.

Found %: C 74.07; H 12.72; OH 13.8. Bromine number 1215. $C_8H_{15}OH$. Calculated %: C 74.94; H 12.58; OH 13.3 Bromine number 1248.

The stated properties are similar to those of 2-ethylhexenol-1, described earlier [1].

The catalytic oxidation of 2-ethylhexenol-1 by air over an incandescent silver wire was attempted. However, it turned out that 2-ethylhexenol-1 in this case easily isomerizes to 2-ethylhexanal. Thus, a single passage of 2--ethylhexenol-1 vapor and air over an incandescent silver wire gave a condensate with an aldehyde content of 42%, calculated as 2-ethylhexanal (by the hydroxylamine method). Treatment of a sample of this condensate with an alcoholic solution of 2,4-dinitrophenylhydrazine gave the 2,4-dinitrophenylhydrazone in the form of yellow needles with m.p. 120.5-121.5° (from alcohol). A sample mixed with 2-ethylhexanal 2,4-dinitrophenylhydrazone did not give a melting-point depression. The dimedon derivative, obtained in aqueous alcohol in the form of long, white needles, had m.p. 191-191.5° (from 50% alcohol), and a sample mixed with the corresponding 2-ethylhexanal derivative did not give a melting-point depression, either.

2-Ethylhexanol-1. For the removal of unsaturated alcohols the 175-182° fraction was treated with a dilute aqueous potassium permanganate solution. On subsequent steam distillation followed by distillation of the alcohol layer which had separated out in the condensate, a product with the following properties was obtained:

b.p. 182-184°, d^{20}_4 0.8325, $n^{20}D$ 1.4325, bromine number 0.

Found %: C 73.31; H 14.07; OH 13.2. $C_8H_{17}OH$. Calculated %: C 73.79; H 13.93; OH 13.1.

On the second isomer of the unsaturated alcohol. In the fractionation of the 175-182° fraction in vacuo with the above-mentioned column, after the separation of fractions of the first isomer of 2-ethylhexenol-1 the bromine numbers of the fractions gradually decreased to 552. Then, as the boiling point rose very slightly, the bromine numbers of the fractions again increased, reaching 752. The last fraction boiled off at 183-185° (752 mm) ($n^{20}D$ 1.4440). A weighed portion of the latter (2.2 g) was hydrogenated with a Raney-nickel catalyst in an ethyl alcohol solution. The amount of H_2 absorbed was 233 ml (S.T.P.). After distillation, the substance obtained had a b.p. of 182-184°, d^{20}_4 0.8320, $n^{20}D$ 1.4322, which corresponds to the constants of 2-ethylhexanol-1.

SUMMARY

The reaction of butyraldehyde with a solution of sodium butoxide in n-butanol has been investigated. It has been shown that in this case two isomers of 2-ethylhexenol-1 are formed, one of which was isolated and proved to be identical with the alcohol isolated earlier from the products of n-butanol condensation.

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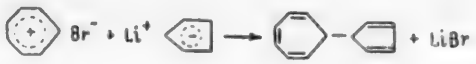
reacted with cyclopentadienyllithium. Here it is not the ionic salt of tropylium with the cyclopentadienyl anion that is formed ($C_7H_7^+C_6H_5^-$), but instead it is the covalent cyclopentadienyl-tropylium (cyclopentadienylcycloheptatriene)* according to the scheme



The formation of a covalent compound is explained by the weakly acidic properties of cyclopentadiene, and consequently by the substantial nucleophilicity of the $C_5H_5^-$ anion.

Tropylium acetate and the benzoate were synthesized by the acylation of tropylium oxide (dicycloheptatrienyl ether) with respectively acetic and benzoic anhydrides according to the scheme

The preparation of cycloheptatrienylium esters by the acylation of tropylium oxide with the corresponding anhydrides can apparently have quite general significance.

Attempts to obtain tropylium acetate by the exchange reaction of tropylium perchlorate with potassium acetate in either water or alcohol proved unsuccessful. In water medium, instead of tropylium acetate, we isolated tropylium oxide. We were also unable to obtain tropylium benzoate either by the exchange reaction of potassium benzoate with tropylium perchlorate in water, or by the exchange decomposition of silver benzoate and tropylium bromide in either alcohol or nitromethane. Instead of tropylium benzoate, we isolated benzoic acid and tropylium oxide. These results are explained by the instability of the cycloheptatrienylium esters and their great tendency to hydrolyze.

Actually, the ester linkage in both the tropylium acetate and benzoate proved to be extremely unstable. Thus, tropylium acetate is readily hydrolyzed by water with the formation of tropylium oxide

$$2C_7H_7{-}OCOCH_3 + H_2O \longrightarrow (C_7H_7)_2O + 2CH_3COOH$$

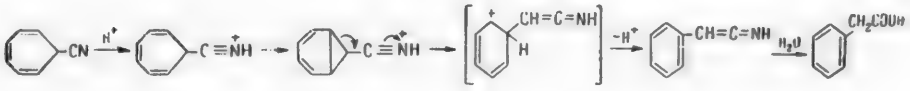
The acetate is instantaneously decomposed by hydrochloric acid with the formation of the tropylium salt. The ester linkage is also easily cleaved when tropylium acetate is treated with dry hydrogen bromide.

The alkaline hydrolysis of tropylium acetate also proceeds with great ease – the compound can be titrated in the cold with alkali solution.

$$2C_7H_7{-}OCOCH_3 + 2NaOH \longrightarrow (C_7H_7)_2O + 2CH_3COONa$$

The covalent bond $C_7H_7{-}X$ in tropylium cyanide and in cyclopentadienyl-tropylium proved to be much more stable. When treated with either hydrogen bromide or with concentrated hydrochloric acid, tropylium cyanide is not converted to the tropylium salt.

It is interesting that in the acid hydrolysis of tropylium cyanide partial isomerization occurs, and phenylacetic acid is formed. Apparently, the isomerization of tropylium cyanide is linked with the formation of the nitrilium salt in acid medium, and the probable mechanism for its formation (by analogy with the mechanisms for the rearrangements of tropolones and tropones [5]) can be depicted by the scheme



*The covalent character of cyclopentadienylheptatriene is also indicated by Doering [6].

EXPERIMENTAL

Tropylium Acetate. To 1.9 g of tropylium perchlorate [3] was added 10 ml of saturated sodium bicarbonate solution. The aqueous solution was extracted with ether, the ether extracts were dried over Na_2SO_4, and the ether was vacuum-distilled. The tropylium oxide obtained in this manner, without further purification, was heated for 1 hour on the water bath with 6 ml of acetic anhydride. Then the acetic anhydride was vacuum-distilled, and the residue was fractionally distilled. We obtained 0.55 g of tropylium acetate (yield 37%, based on tropylium perchlorate); b.p. 52-55° (1 mm), $n^{19}D$ 1.5397, d^{20}_4 1.083.

Found %: C 72.28, 72.18; H 6.49, 6.49; $C_9H_{10}O_2$. Calculated %: C 71.98; H 6.71.

Tropylium acetate is readily soluble in ether, benzene, petroleum ether and carbon tetrachloride. It rapidly darkens in the air.

A solution of 0.0573 g of tropylium acetate in 3 ml of dry carbon tetrachloride was saturated with dry hydrogen bromide. Here a yellow precipitate of tropylium bromide was obtained. The bromide was dissolved in alcohol and then treated with chloroplatinic acid to give 0.0661 g of tropylium chloroplatinate; yield 60%.

0.3432 g of tropylium acetate was dissolved in 3 ml of concentrated hydrochloric acid. The addition of chloroplatinic acid gave 0.4576 g of tropylium chloroplatinate; yield 68%.

A solution of 0.0941 g of tropylium acetate in alcohol was titrated with 0.1 N alcoholic NaOH solution using phenolphthalein as indicator. The amount of alkali consumed for the titration was 5.1 ml (81% of the theoretical).

Tropylium Benzoate. To the tropylium oxide obtained from 4.75 g of tropylium perchlorate was added a solution of 1.5 g of benzoic anhydride in absolute ether. The mixture was boiled for 30 minutes, the ether was distilled off, anhydrous benzene was added to the residue, and the boiling was continued for another 1.5 hours. Vacuum-distillation gave 0.31 g of tropylium benzoate with b.p. 76-82° (2 mm); yield 11% (calculated on the benzoic anhydride).

Found %: C 79.56, 79.44; H 5.92, 5.82. $C_{14}H_{12}O_2$. Calculated %: C 79.22; H 5.70.

Tropylium benzoate is readily soluble in nonpolar solvents; it darkens rapidly in the air.

Hydrolysis of Tropylium Cyanide. A mixture of 0.9 g of tropylium cyanide [obtained from the reaction of 1.9 g of tropylium perchlorate with 1 g of KCN in 25 ml of water; b.p. 51-53° (1.5 mm), $n^{20}D$ 1.5310, d^{20}_4 1.017] and 4 ml of concentrated hydrochloric acid was refluxed for 2 hours. The solution was extracted with ether. The ether extracts were extracted with 10% NaOH solution, which was then acidified with hydrochloric acid and again extracted with ether. This purification procedure was repeated twice. The ether extracts were dried and evaporated. The residue was extracted with petroleum ether, from which 0.08 g of phenylacetic acid with m.p. 76° was isolated; the latter does not depress the melting point with the authentic specimen.

Cyclopentadienylcycloheptatriene. To 0.4 g of freshly distilled cyclopentadiene was added a solution of butyllithium (from 0.9 g of n-C_4H_9Br and 0.15 g of Li). To the obtained suspension of cyclopentadienyllithium was added 0.75 g of finely pulverized tropylium bromide, and the mixture was stirred for 1 hour. Then the ether was distilled off, and the residue was extracted with petroleum ether. Removal of the petroleum ether by distillation, followed by vacuum-distillation, gave cyclopentadienylcycloheptatriene with b.p. 82-84° (4 mm); yield 0.44 g (56%, based on tropylium bromide); $n^{20}D$ 1.5610. The compound is readily soluble in ether, benzene and petroleum ether, and insoluble in water; it does not give a precipitate of tropylium chloroplatinate when treated with H_2PtCl_6.

SUMMARY

1. Tropylium acetate, tropylium benzoate and cyclopentadienylcycloheptatriene were synthesized, proving to be covalent compounds.

2. It was shown that the character of the bond between the cycloheptatrienylium radical and the anion depends on the degree of nucleophilicity shown by the anion. The transition from ionic to covalent derivatives of tropylium lies in the K_a limits of $1.2 \cdot 10^{-4}$ to $6.3\text{-}1.75 \cdot 10^{-5}$.

3. It was shown that rearrangement occurs during the acid hydrolysis of tropylium cyanide with the formation of phenylacetic acid.

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SIMULTANEOUS HYDROLYSIS OF MONO- AND TRIFUNCTIONAL ALKYL(ARYL)CHLOROSILANES

K. A. Andrianov, M. Ia. Levshuk, S. A. Golubtsov and T. A. Krasovskaia

The synthesis of most polymeric organosilicon compounds of the polyorganosiloxane type is accomplished by the method of simultaneous hydrolysis of two, and at times of a greater number of monomeric organosilicon compounds, represented by the alkyl- or arylchlorosilanes, or by the substituted esters of orthosilicic acid. There is very little information in the literature regarding the simultaneous hydrolysis of the indicated monomers. It is usually assumed that when a mixture of two alkyl- or arylchlorosilanes is hydrolyzed it is the polymeric product of the simultaneous hydrolysis of these two compounds that is formed. In studying this process for mixtures of compounds with different functionality, we found that this reaction goes in part toward the formation of not the simultaneous hydrolysis product, but instead to a mixture of the two polymers. Thus, for example, when we attempted to prepare polymers with a branched-chain structure from an aryltrichlorosilane and triethylchlorosilane by scheme (1) we found that if the reaction was run at a temperature not exceeding 20° the hydrolysis product was a mixture of hexaethyldisiloxane and tarry phenylsiloxane polymer, formed according to schemes (2) and (3).

$$(x+2)(C_2H_5)_3SiCl + xRSiCl_3 \xrightarrow{H_2O} (C_2H_5)_3SiO\left[\begin{array}{c} RSiO \\ | \\ O \\ | \\ Si(C_2H_5)_3 \end{array}\right]_x Si(C_2H_5)_3 \qquad (1)$$

where $R = C_6H_5$ or C_6H_4Cl.

$$2(C_2H_5)_3SiCl \xrightarrow{H_2O} (C_2H_5)_3SiOSi(C_2H_5)_3 \qquad (2)$$

$$xRSiCl_3 \xrightarrow{H_2O} (RSiO_{1,5})_x \qquad (3)$$

As our experiments revealed, neitherchanging the molar ratios nor the acidity of the medium, nor using various solvents during hydrolysis, made it possible to suppress reactions (2 and (3), and direct the process toward

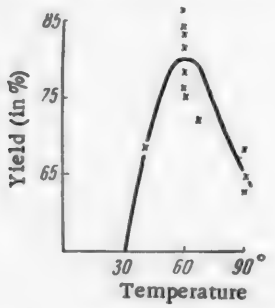

Fig. 1. Simultaneous hydrolysis of phenyltrichlorosilane and triethylchlorosilane.

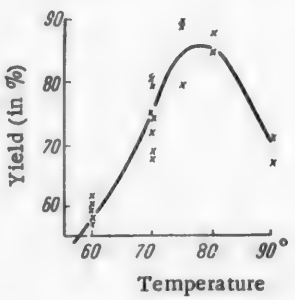

Fig. 2. Simultaneous hydrolysis of chlorophenyltrichlorosilane and triethylchlorosilane.

the formation of the simultaneous hydrolysis product according to reaction (1). Quite probably this is due to the existence of considerable differences in the hydrolysis and condensation rates of compounds with different functionality.

TABLE 1

Simultaneous Hydrolysis of Phenyltrichlorosilane and Triethylchlorosilane

Change (in g)		g-moles triethylchlorosilane per g-mole phenyltrichlorosilane	Temperature	Yield of hydrolysis product (in g)	Yield (in %)	
phenyltrichlorosilane	triethylchlorosilane				cohydrolysis product	still residue
18.7	40	3.0	4°	39	Absent	23.8*
18.7	40	3.0	20	41	Absent	24.7*
18.7	80	6.0	20	71	Absent	25.3*
18.7	40	3.0	40	42	68	12.6
18.7	40	3.0	60	42	78	9.4
148	348	3.3	60	351	76	20.0
148	348	3.3	60	359	81	12.0
106	340	4.5	60	396	75	16.0
211	677	4.5	60	666	84	11.0
106	451	6.0	60	410	86	Traces
211	903	6.0	60	805	83	7.2
106	248	3.3	70	314	73	8.0
18.7	40	3.0	90	39	65	9.0
106	452	6.0	90	412	63	12.0
106	226	3.0	90	262	67	17.0

TABLE 2

Simultaneous Hydrolysis of Chlorophenyltrichlorosilane and Triethylchlorosilane

Change (in g)		g-moles triethylchlorosilane per g-mole phenyltrichlorosilane	temp.	Yield of hydrolysis product (in g)	Yield (in %)	
chlorophenyltrichlorosilane	triethylchlorosilane				cohydrolysis product	still residue
24.6	67.7	4.5	60°	66	70	71
24.6	67.7	4.5	60	76	61	26
54.1	109	3.3	60	102	61	12
73.8	148	3.3	60	150	62	27
73.8	148	3.3	60	149	60.5	19
123.5	226	3.0	60	343	58.6	23
123	226	3.0	60	266	50	33
173	348	3.3	60	398	63	30
173	348	3.3	60	—	60	29
369	745	3.3	70	969	69	21
73.8	149	3.3	70	165	76	11
73.8	203	4.5	70	219	80	18
73.8	203	4.5	70	231	73	9
73.8	149	3.3	70	191	81	17
73.8	203	4.5	70	192	68	6
73.8	149	3.3	70	168	75	9
73.8	149	3.3	75	170	89	7
213	430	3.3	75	540	80	8
246	677	4.5	75	709	90	7
73.8	149	3.3	80	187	88	11
73.8	149	3.3	80	173	86	11
246	677	4.5	80	704	85	6
73.8	149	3.3	90	—	72	14
73.8	149	3.3	90	149	68	12

*Hard tar.

It was natural to assume that the temperature coefficients of the rates of the indicated reactions are different; for this reason we attempted to accomplish the simultaneous hydrolysis of compounds with different functionality by varying the reaction temperature. Experiment revealed that the assumption made is valid, and that running the hydrolysis at elevated temperature favors obtaining simultaneous hydrolysis products, and not a mechanical mixture of the two polymers.

The relationship between the yield of simultaneous hydrolysis product and the reaction temperature for the case of the hydrolysis of a mixture of phenyltrichlorosilane and triethylchlorosilane is shown in Fig. 1. The optimum temperature for running the process according to scheme (1) is 60°. A similar relationship between the yield of cohydrolysis product and the temperature for a mixture of chlorophenyltrichlorosilane and triethylchlorosilane is shown in Fig. 2 (in this case the optimum temperature for simultaneous hydrolysis is 90°).

EXPERIMENTAL

Water was placed in a round-bottomed flask, fitted with dropping funnel, thermometer, stirrer and reflux condenser, and its temperature was brought up to the reaction temperature by heating the flask on the water bath. A mixture of triethylchlorosilane and phenyltrichlorosilane (molar ratio 3 : 1) was then added to the flask with stirring and at a constant temperature. The hydrolysis product was separated from the hydrochloric acid, washed, dried, and heated at 200° for 1 hour, after which it was fractionally distilled at a pressure of 2 mm. The 80-110° fraction proved to be hexaethyldisiloxane; the 110-250° fraction was the liquid product of simultaneous hydrolysis. The residue was a liquid high-molecular product of incomplete cohydrolysis, or if the reaction was run at low temperature it represented solid phenylsiloxane polymer. The yield of simultaneous hydrolysis products was calculated in percent of the theoretical according to reaction (1), after substracting the hexaethyldisiloxane. The results of the experiments on the simultaneous hydrolysis of mixtures of phenyltrichlorosilane and triethylchlorosilane at various temperatures are shown in Table 1, while the results of the experiments on the hydrolysis of mixtures of chlorophenyltrichlorosilane and triethylchlorosilane, run by a similar procedure, are shown in Table 2.

SUMMARY

It was established that when the hydrolysis of mixtures of mono- and trifunctional alkyl(aryl)chlorosilanes (phenyl- or chlorophenyltrichlorosilane with triethylchlorosilane) is run at room temperature the reaction product is a mixture of the two polymers (hexaethyldisiloxane and polyphenylsiloxane resin). The product of the simultaneous hydrolysis of phenyl- or chlorophenyltrichlorosilane with triethylchlorosilane is formed if the reaction is run at elevated temperature.

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SYNTHESIS AND PROPERTIES OF TETRAKIS(TRIBENZYLSILOXY)SILANE AND TETRAKIS(TRIBENZYLSILOXY)METHANE

V. S. Chugunov

Tetrakis(triarylsiloxy)silanes of type $[Ar_3SiO]_4Si$ and their corresponding analogs – the tetrakis(triarylsiloxy)-methanes – have not been reported up to now. In one of our studies [1] it was established that the reaction of excess sodium triphenylsilanolate with either silicon tetrachloride or tetrafluoride, due to the high steric hindrance shown by the triphenylsiloxy group, yields only the corresponding tris(triphenylsiloxy)halosilane of type $[Ar_3SiO]_3SiX$.

In the present study a substitution of the less sterically hindered benzyl radicals for the phenyl radicals enabled us to successfully accomplish the synthesis of tetrakis(tribenzylsiloxy)silane according to the equation

$$4(C_6H_5CH_2)_3SiONa + SiCl_4 \rightarrow [(C_6H_5CH_2)_3SiO]_4Si + 4NaCl$$

This compound was obtained as colorless crystals with m.p. 204-205°, and stable to both dilute acids and alkalies.

Under similar conditions, starting with sodium tribenzylsilanolate and carbon tetrabromide, we obtained tetrakis(tribenzylsiloxy)methane with m.p. 217-218° in 42% yield.

Using a spectrometer with NaCl prism we investigated* the infrared absorption spectra of tetrakis(tribenzylsiloxy)silane and tetrakis(tribenzylsiloxy)methane, pelleted with potassium bromide powder, in the 6-15 μ region.

The frequencies (in cm^{-1}) of the absorption bands and the conjectural interpretation of some of them are given below.

Next, starting with sodium triphenylsilanolate and carbon tetrabromide, we obtained tris(triphenylsiloxy)bromomethane with m.p. 231-232°. The tris(triphenylsiloxy)methane obtained by us earlier [2] had m.p. 222-223°.

It was shown that the Si–O–Si bond in tris(triphenylsiloxy)halosilanes is more resistant to the action of alkali solution than is the Si–O–C bond in the similarly constructed tris(triphenylsiloxy)bromomethane. Thus, when tris(triphenylsiloxy)bromomethane is treated with alkali the Si–O–C bond suffers rupture with the formation of triphenylsilanol according to the equation

$$[(C_6H_5)_3SiO]_3CBr \xrightarrow[HOH]{NaOH} 3(C_6H_5)_3SiOH$$

At the same time, the Si–O–Si bond in either tris(triphenylsiloxy)chlorosilane or tris(triphenylsiloxy)fluorosilane remains unchanged under the above indicated conditions, and only as the result of halogen hydrolysis is the corresponding tris(triphenylsiloxy)silanol formed [1].

EXPERIMENTAL

The tribenzylsilanol used as starting product was obtained by the saponification of tribenzylfluorosilane, obtained [3] by the reaction of benzylmagnesium chloride with silicon tetrafluoride, in alcohol-ether mixture with 2 N caustic solution.

* The author wishes to thank A. N. Lazarev for taking the infrared absorption spectra.

$[(C_6H_5CH_2)_2SiO]_4Si$	$[(C_6H_5CH_2)_2SiO]_4C$	Interpretation
1610 (m)	1620 (v w)	Valence vibrations of the C_6H_5 ring
1470 (s)	1470 (w)	
1447 (s)	1427 (s)	Deformations of the CH_2 group
1397 (m)	1385 (w)	
1208 (s)	1191 (m)	Vibrations of the $-\overset{|}{\underset{|}{Si}}-C$ group
1161 (s)	1151 (m)	Vibrations of the C_6H_5 group
—	1117 (v w)	Valence vibrations of C—O
1092 (vs)	1092 (vw)	Valence vibrations of Si—O
1056 (m)	1070—1050 (m)	Vibrations of the C_6H_5 group and the C—C bond
1027 (m)	1027 (m)	
997 (m)	995 (m)	
968 (m)		
907 (s)	918 (vw)	
848 (m)	856 (w)	
822 (s)	—	
810 (s)	—	
780 (vs)	—	
763 (s)	—	
746 (m)	743 (m)	Nonplanar CH deformations of the C_6H_5 group
737 (m)	736 (s)	
—	708 (vs)	
693 (s)	694 (s)	Nonplanar CH deformations of the C_6H_5 group

Legend. 1. The intensity characteristics of the bands are given in parentheses: vs — very strong, s — strong, m — medium, w — weak, vw — very weak.
2. Some of the bands in the 690-750 cm^{-1} region may be due to Si—C vibrations.
3. Some weak bands were observed in the 1325-1240 cm^{-1} region, caused by trace impurities in the KBr.

Tetrakis(tribenzylsiloxy)silane. In a flask, fitted with reflux condenser, was placed 32 g of tribenzylsilanol, dissolved in 300 ml of dry benzene, and 3 g of sodium metal; the flask contents were heated under reflux for 2 hours, and after the sodium tribenzylsilanolate had formed the solution was cooled to 5-7°, a solution of 4.2 g of silicon tetrachloride in 50 ml of benzene added, and the mixture heated an additional 4 hours under reflux. After separating the formed sodium chloride the isolated crystals were recrystallized twice from benzene. We obtained 24.2 g of coarse transparent crystals (yield 75.4%, based on silicon tetrachloride); m.p. 204-205°.

Found %: Si 10.2, 10.5. $C_{84}H_{84}O_4Si_5$. Calculated %: Si 10.8.

Tetrakis(tribenzylsiloxy)methane. Sodium tribenzylsilanolate was prepared from 16 g of tribenzylsilanol, 200 ml of benzene and 2 g of sodium. To the solution, cooled to 0°, was added 4 g of carbon tetrabromide, dissolved in 100 ml of benzene; the mixture was heated under reflux for 8 hours. After separating the sodium bromide the isolated crystals were recrystallized from benzene. Transparent crystals. Yield 6.5 g (42%, based on carbon tetrabromide); m.p. 217-218°.

Found %: C 80.2, 80.3; Si 8.5, 8.5; H 6.9, 7.0. $C_{85}H_{84}O_4Si_4$. Calculated %: C 79.7; Si 8.8; H 6.6.

Tris(triphenylsiloxy)bromomethane. Sodium triphenylsilanolate was prepared from 27.6 g of triphenylsilanol in 300 ml of benzene and 3 g of sodium. To the solution, cooled to 0°, was added 4 g of carbon tetrabromide in 50 ml of benzene; the mixture was heated under reflux for 8 hours. After separating the sodium bromide the isolated crystals were recrystallized from benzene. Yield 4.7 g (30.2%, based on carbon tetrabromide). Fine crystals; m.p. 231-232°.

Found %: Si 8.0, 7.8; Br 7.1, 7.3. $C_{64}H_{63}O_3BrSi_3$. Calculated %: Si 8.1, Br 7.6.

Reaction of Tris(triphenylsiloxy)bromomethane With Alkali. In a flask, fitted with reflux condenser, was placed 1.84 g of tris(triphenylsiloxy)bromomethane in 50 ml of dioxan and 5 ml of 2 N NaOH; the mixture was heated under reflux on the water bath for 2 hours. Then the solution was treated with 50 ml of water and the ob-

tained flocculent precipitate was filtered and recrystallized from ether. We obtained 1.32 g of triphenylsilanol, identified by its melting point.

SUMMARY

1. The previously unknown tetrakis(tribenzylsiloxy)silane and tetrakis(tribenzylsiloxy)methane were synthesized and their infrared absorption spectra investigated.

2. It was shown that the Si—O—C bond in tris(triphenylsiloxy)bromomethane is less stable to the action of alkali solution than is the Si—O—Si bond in tris(triphenylsiloxy)halosilanes.

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TRIMETHOXY- AND TRIARYLOXYPHOSPHAZOSULFONITROPHENYLS AND DIESTERS OF NITROPHENYLSULFONAMIDOPHOSPHORIC ACIDS

A. V. Kirsanov and N. G. Feshchenko

The trimethoxy- and triaryloxyphosphazosulfonitrophenyls (I) and the diesters of nitrophenylsulfonamidophosphoric acids (II) were synthesized for the purpose of studying their insecticidal properties and as starting substances for the preparation of N-phosphoric acid derivatives of sulfanilamides.

Compounds of type (I) were obtained by the reaction of trichlorophosphazosulfonitrophenyls [1] with either sodium methylate or arylate in benzene solution [2] according to the scheme

$$NO_2C_6H_4SO_2N{=}PCl_3 + 3NaOR \longrightarrow 3NaCl + NO_2C_6H_4SO_2N{=}P(OR)_3$$

In this manner we obtained the trimethoxy-, triphenoxy-, tris(p-chlorophenoxy)-,tris(o-nitrophenoxy)- and tris(p-nitrophenoxy)-phosphazosulfo-o-, m- and p-nitrophenyls (I) (Table 1).

Compounds of type (I) are colorless crystalline compounds of a neutral character, insoluble in water. The trimethoxyphosphazosulfonitrophenyls (III) when boiled with 96% alcohol for 1 hour are saponified to the corresponding diesters (XIV). The triphenoxyphosphazosulfonitrophenyls (IV) do not change under these conditions. The trimethoxy- and triphenoxyphosphazosulfonitrophenyls have comparatively low melting points (in the range 56-104°). Compounds of type (I) are not saponified when treated with aqueous alkali solutions, which is explained by their insolubility in water. In aqueous-alcohol alkali solutions they are easily saponified to (II). However, compounds of the (II) type are obtained more conveniently from the dichlorides of nitrophenylsulfonamidophosphoric acids [1] by reaction with sodium methylate or arylates in dioxan solution by the scheme

$$NO_2C_6H_4SO_2NHPOCl_2 + 3NaOR \longrightarrow 3NaCl + ROH +$$
$$+ [NO_2C_6H_4SO_2NPO(OR)_2]^-Na^+ \xrightarrow{+H^+} NO_2C_6H_4SO_2NHPO(OR)_2$$

In this manner we obtained the dimethyl, diphenyl, di-(p-chlorophenyl), di-(o-nitrophenyl) and di-(p-nitrophenyl) esters of the o-, m- and p-nitrophenylsulfonamidophosphoric acids (II) (Table 2). It is possible to isolate the (II) compounds as the salts, but it is more convenient to isolate them as the free diesters. The (II) compounds are comparatively high-melting (in the range 134-194°), colorless, crystalline substances, insoluble in water, and melting considerably higher than the corresponding (I) compounds, with the exception of the two p-nitrophenol esters (XI and XIII), which melt below the corresponding (I) compounds. The (II) compounds are monobasic acids, capable of being titrated accurately in the presence of phenolphthalein, and giving sodium salts that crystallize well and are readily soluble in water. It is interesting to mention that the sodium salts of the p-chlorophenyl esters of nitrophenylsulfonamidophosphoric acids, when their aqueous solutions are extracted with ether, pass almost entirely into the ether layer. The sodium salts of the other diesters are not extracted from their aqueous solutions by ether.

EXPERIMENTAL

Trimethoxyphosphazosulfonitrophenyls (III). To a solution of 0.06 g-mole of sodium methylate in 30 ml of methanol, cooled to 0°, was slowly added with mechanical stirring a solution of 0.02 g-mole of trichlorophosphazosulfonitrophenyl in 40 ml of benzene at such a rate that the temperature was maintained in the range 0 to +5°. After all of the solution of phosphazo compound had been added, the reaction mixture was heated at 50° for 30 minutes. The solvents were removed by distillation in vacuo, the residue was treated with 40 ml of water, and

TABLE 1

Trimethoxy- and Triaryloxyphosphazosulfonitroaryls (I) of Type $ArC_6H_4SO_2N{=}P(OR)_3$

Number of compound	Ar	R	Yield (in %)	Crystalline form, solvent	Melting point	Formula	N (in %) found	N (in %) calculated
III	o-$NO_2C_6H_4$	CH_3	80.0	Needles from CCl_4	68—70°	$C_9H_{13}O_7N_2SP$	8.67	8.64
III	m-$NO_2C_6H_4$	CH_3	81.3	Needles from CCl_4	57—59		8.72	8.64
III	p-$NO_2C_6H_4$	CH_3	88.7	Needles from CCl_4	94—96		8.78	8.64
IV	o-$NO_2C_6H_4$	C_6H_5	84.2	Prisms from alcohol	78—79	$C_{24}H_{19}O_7N_2SP$	5.62	5.49
IV	m-$NO_2C_6H_4$	C_6H_5	81.0		56—58		5.47	5.49
IV	p-$NO_2C_6H_4$	C_6H_5	80.0	Prisms from alcohol	101—104		5.66	5.49
V	o-$NO_2C_6H_4$	p-ClC_6H_4	70.0	Needles from CCl_4	139—141	$C_{24}H_{16}O_7N_2Cl_3SP$	4.58	4.56
V	m-$NO_2C_6H_4$	p-ClC_6H_4	75.0	Prisms from alcohol	133—135		4.64	4.56
V	p-$NO_2C_6H_4$	p-ClC_6H_4	64.2	Needles from CCl_4	151—153		4.56	4.56
VI	o-$NO_2C_6H_4$	o-$NO_2C_6H_4$	90.0	Prisms from benzene	140—141	$C_{24}H_{16}O_{13}N_5SP$	10.83	10.83
VI	m-$NO_2C_6H_4$	o-$NO_2C_6H_4$	82.0	Prisms from benzene	135—137		10.91	10.83
VI	p-$NO_2C_6H_4$	o-$NO_2C_6H_4$	95.0	Prisms from benzene	159—161		10.76	10.83
VII	o-$NO_2C_6H_4$	p-$NO_2C_6H_4$	79.0	Needles from dioxan	199—202		10.91	10.83
VII	m-$NO_2C_6H_4$	p-$NO_2C_6H_4$	83.0	Prisms from benzene	175—177		10.73	10.83
VII	p-$NO_2C_6H_4$	p-$NO_2C_6H_4$	85.0	Prisms from acetone	202—203		10.82	10.83

the obtained crystalline precipitate was suction-filtered, washed with water, and air-dried. The trimethoxyphosphazosulfo-m-nitrophenyl deposited as an oil, which was extracted with benzene. Removal of the benzene by distillation left a viscous oil, which soon crystallized completely.

Triphenoxyphosphazosulfonitrophenyls (IV) and Tris(p-chlorophenoxy)phosphazosulfonitrophenyls (V). To 0.045 g-mole of well-dried and pulverized sodium phenate or sodium p-chlorophenate was added in one portion a solution of 0.015 g-mole of trichlorophosphazosulfonitrophenyl in 30 ml of dry benzene and the mixture was stirred vigorously. When stormy reaction had ended, the mixture was heated under reflux on the water bath for 1 hour. The benzene was distilled in vacuo and the residue was treated with 25 ml of 1 N aqueous sodium hydroxide solution. Here (V) and (VIII) deposited immediately as crystalline precipitates. The triphenoxyphosphazosulfo-o-nitrophenyl deposited as an oil, which crystallized completely when rubbed with a glass rod. The triphenoxyphosphazosulfo-m-nitrophenyl was synthesized by a similar procedure, but in dioxan solution.

Tris(o-nitrophenoxy)- (VI) and Tris(p-nitrophenoxy)-phosphazosulfonitrophenyls (VII). The reaction was run in the same manner as for (IV) and (V), but here it is necessary to heat the reaction mixture under reflux and with stirring for not less than 5 hours. After removal of the benzene by distillation in vacuo the residue was treated with 25 ml of 1 N caustic solution, the crystalline precipitate suction-filtered, and then washed 3 times each with water, alcohol and ether to remove free nitrophenol. The (VI) and (VII) compounds obtained in this manner are practically pure and melt within three degrees. All the (I) compounds are insoluble in water, ether and petroleum ether, and readily soluble at room temperature in acetone and dioxan, with the exception of (VIII) and (XI), which dissolve in dioxan only on heating. (III) and (IV) are readily soluble in ethyl acetate, and can be recrystallized from either alcohol or benzene. The (VI) compounds are insoluble in alcohol, and can be recrystallized from benzene. (VI) and (VII) are insoluble in carbon tetrachloride, (III) and (IX) are slightly soluble, and (IV), (VIII) and (X) are somewhat soluble in this solvent.

TABLE 2

Dimethyl and Diaryl Esters of Nitrophenylsulfonamidophosphoric Acids (II) of Type $ArSO_2NHPO(OR)_2$

Number of compound		Ar	R	Yield (in %)	Recrystallization solvent	Melting point	Formula	N (in %) found	N (in %) calculated	No. of equivalents found	No. of equivalents calculated
XIV	XIX	o-$NO_2C_6H_4$	CH_3	80.0	benzene	134—136°	$C_8H_{11}O_7N_2SP$	9.18	9.03	1.004	1.000
	—	m-$NO_2C_6H_4$	CH_3	87.0	alcohol	145—148		9.17	9.03	1.008	1.000
	XX	p-$NO_2C_6H_4$	CH_3	82.3	alcohol	175—177		8.98	9.03	1.008	1.000
XV	—	o-$NO_2C_6H_4$	C_6H_5	84.5	benzene	156—158	$C_{18}H_{15}O_7N_2SP$	6.55	6.45	1.003	1.000
	—	m-$NO_2C_6H_4$	C_6H_5	83.7	benzene	146—147		6.58	6.45	0.990	1.000
	—	p-$NO_2C_6H_4$	C_6H_5	88.2	benzene	192—193		6.45	6.45	1.010	1.000
XVI	XXI	o-$NO_2C_6H_4$	p-ClC_6H_4	70.0	benzene	149—151	$C_{18}H_{13}O_7N_2Cl_2SP$	5.60	5.56	1.020	1.000
	—	m-$NO_2C_6H_4$	p-ClC_6H_4	70.5	benzene	153—155		5.71	5.56	1.008	1.000
	—	p-$NO_2C_6H_4$	p-ClC_6H_4	80.0	benzene	163—165		5.63	5.56	1.005	1.000
XVII	—	o-$NO_2C_6H_4$	o-$NO_2C_6H_4$	71.0	alcohol	171—174	$C_{18}H_{13}O_{11}N_4SP$	10.64	10.69	1.000	1.000
	—	m-$NO_2C_6H_4$	o-$NO_2C_6H_4$	72.5	alcohol	175—178		10.76	10.69	1.006	1.000
	—	p-$NO_2C_6H_4$	o-$NO_2C_6H_4$	71.6	water	167—170		10.69	10.69	1.010	1.000
XVIII	—	o-$NO_2C_6H_4$	p-$NO_2C_6H_4$	74.2	alcohol	188—191		10.71	10.69	1.014	1.000
	—	m-$NO_2C_6H_4$	p-$NO_2C_6H_4$	87.8	alcohol	191—194		10.78	10.69	1.005	1.000
	XXII	p-$NO_2C_6H_4$	p-$NO_2C_6H_4$	89.2	Na salt was reprecipitated	165—168		10.77	10.69	1.020	1.000

(VII), (VIII), and (X) are difficultly soluble in alcohol, and (IX) is somewhat more soluble. (X), (XI) and (XIII) are difficultly soluble in benzene, and (VII), (IX) and (XII) are much more soluble in this solvent. Thus, the solubility of (III), (IV) and (VI) is determined mainly by the nature of the ester groups (OR) and changes but slightly when the position of the nitro group in the nitroarylsulfonyl grouping ($NO_2C_6H_4SO_2$) is changed. In the case of the p-chlorophenol (V) and p-nitrophenol (VII) derivatives the position of the nitro group in $NO_2C_6H_4SO_2$ exerts a very great influence on the solubility. The p-nitrophenol derivatives (VII) are the most difficultly soluble in the common organic solvents.

Dimethyl Esters of Nitrophenylsulfonamidophosphoric Acids (XIV). To a solution of 0.06 g-mole of sodium methylate in 35 ml of methanol, with ice-water cooling and vigorous stirring, was added 0.02 g-mole of finely pulverized nitrophenylsulfonamidophosphoryl dichloride. On conclusion of quite violent reaction the mixture was boiled for 10 minutes under reflux, the benzene was vacuum-distilled, and the residue, a mixture of sodium salt (XIV) and sodium chloride, was treated with 20 ml of 2 N hydrochloric acid. Here (XIV) deposited as an oil, which crystallized completely when cooled and rubbed with a glass rod. The product was suction-filtered, washed with cold water, and air-dried.

Diphenyl (XV), Di(p-chlorophenyl) (XVI), Di(o-nitrophenyl) (XVII) and Di(p--nitrophenyl) (XVIII) Esters of Nitrophenylsulfonamidophosphoric Acids. To 0.06 g--mole of well-dried and pulverized sodium arylate was added with stirring a solution of 0.02 g of nitrophenylsulfonamidophosphoryl dichloride in 40 ml of dioxan, and this was accompanied by considerable heat evolution. The mixture was boiled under reflux with stirring for 1 hour in the case of (XV), for 3 hours in the case of (XVI), and for 6 hours in the case of (XVII) and (XVIII). Then the solvent was removed by distillation in vacuo, the residue, representing a mixture of diester sodium salts, sodium chloride and the phenol, was dissolved in water, and the obtained solution extracted with ether (3 times

with 15-ml portions) to remove the phenol formed in the reaction. The water layer was filtered and then acidified with hydrochloric acid until acid to Congo, and here the free diesters deposited either as needlelike crystals or as an oil, which soon crystallized completely. In the case of (XVI) the ether extracted almost all of the diester sodium salt from the water solution, and for this reason the dry residue obtained after evaporation of the ether was treated with 20 ml of 2 N hydrochloric acid, then with 30 ml ether, and the whole shaken vigorously. Three layers were formed when this was done – an aqueous layer, an ether layer, and an oil layer containing the free (XVI) compounds, which on shaking soon crystallized as coarse needles. The product was suction-filtered, washed with water and ether, and then air-dried.

All the (II) compounds are readily soluble in acetone at 20°, readily soluble in boiling alcohol, and insoluble in cold water, ether, carbon tetrachloride and petroleum ether. (XVII), (XVIII), (XIX) and (XX) are readily soluble in hot water, while the (XVI) compounds are only slightly soluble. The (XVI) compounds are readily soluble in boiling benzene, while (XVII) and (XVIII) are insoluble in benzene. All the (II) compounds crystallize as needles. All the (II) compounds give well crystallizing salts when treated with 1 equivalent of caustic solution. Thus, for example, (XXII) gives the sodium salt of the di(p-nitrophenyl) ester of p-nitrophenylsulfonamidophosphoric acid (XXIII), readily soluble in water, and crystallizing from alcohol as coarse needles (m.p. 220-222°).

Found %: N 10.21. $C_{18}H_{12}O_{11}N_4SPNa$. Calculated %: N 10.26.

The treatment of (XXIII) with mineral acids yields (XXII).

SUMMARY

The trimethoxy- and triaryloxyphosphazosulfonitrophenyls and the dimethyl and diaryl esters of nitrophenylsulfonamidophosphoric acids were obtained and described.

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SUBSTITUTED IMIDO- AND MONOARYLSULFAMIDES

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Earlier imidosulfamide was a practically unavailable substance [1], while the substituted imidosulfamides were not known. At the present time imidosulfamide is quite readily available [2], and the 3-methyl- and 3-ethylimidosulfamides have been obtained from it [3]. The 1- and 1,5-substituted imidosulfamides have been unknown up to now.

The free imidosulfamide in its chemical properties is a monobasic acid, in strength almost equal to that of either sulfuric or hydrochloric acid [2]. For this reason the 3-substituted derivatives of imidosulfamide [3] should be called esters of imidosulfamide, which is in accord with their chemical properties, and only the 1- and 1,5--substituted imidosulfamides should be regarded as being substituted imidosulfamides.

A second method for the preparation of imidosulfamide [2] proved suitable for the preparation of the 1,5-disubstituted and 1,1,5,5-tetrasubstituted imidosulfamides, and consequently this method is a general method for the preparation of not only the unsubstituted, but also the 1,5-di- and 1,1,5,5-tetrasubstituted imidosulfamides, according to the scheme

$$2R_2NSO_2NH_2 + OH^- \rightarrow NH_3 + H_2O + (R_2NSO_2NSO_2NR_2)^-,$$

where R can be hydrogen, an alkyl or an aryl.

Using this scheme the sodium salts are obtained in very good yields, and from them the free 1,1,5,5-tetramethylimidosulfamide (I) and 1,5-diphenylimidosulfamide (II). In their chemical properties (I) and (II) are very similar to the unsubstituted imidosulfamide [2]. They represent colorless crystalline compounds, are strong monobasic acids, and when boiled with water for a short time they suffer complete hydrolysis with the formation of the corresponding substituted sulfamines and substituted sulfamic acids. In the case of 1,5-diphenylimidosulfamide the unstable phenylsulfamic acid [4] formed at first is immediately hydrolyzed to aniline acid sulfate

$$C_6H_5NHSO_2NHSO_2NHC_6H_5 \xrightarrow{+H_2O} C_6H_5NHSO_2NH_2 + C_6H_5NHSO_2OH \xrightarrow{+H_2O}$$
$$\rightarrow C_6H_5NH_2 \cdot H_2SO_4 \quad \text{(III)}$$

The formation of (I) and (II) from N,N-dimethylsulfamide and N,N'-diphenylsulfamide shows very clearly that the scheme proposed for the formation of imidosulfamide from sulfamide by treatment of the latter with caustic alkalies [2] is completely incorrect. The formation of (I) makes the following direct scheme more probable

$$(CH_3)_2NSO_2NH_2 + OH^- \rightleftarrows H_2O + (CH_3)_2NSO_2NH^-$$

$$(CH_3)_2NSO_2NH^- + NH_2SO_2N(CH_3)_2 \rightarrow \left[(CH_3)_2NSO_2NH-\overset{\displaystyle O}{\overset{\|}{S}}(NH_2)(O)-N(CH_3)_2\right]^- \rightarrow$$

$$\rightarrow NH_3 + [(CH_3)_2NSO_2NSO_2N(CH_3)_2]^-$$

The formation of imidosulfamide from sulfamide and tertiary bases can proceed according to the scheme

$$NH_2SO_2NH_2 + Py \rightleftarrows PyH^+ + NH_2SO_2NH^-, \text{ etc.}$$

Since the formation of imidosulfamide, even if only in small yield, is also observed when sulfamide is heated without catalysts, the possibility is not excluded that the initial addition product is formed according to the scheme

$$NH_2SO_2NH_2 + NH_2SO_2NH_2 \longrightarrow \left[NH_2SO_2NH_2^+ - \underset{\underset{NH_2}{\diagup}\quad\underset{O^-}{\diagdown}}{\overset{\overset{O}{\|}}{S}} - NH_2 \right] \longrightarrow$$

$$\longrightarrow NH_3 + NH_2SO_2NHSO_2NH_2,$$

and then the reaction is catalyzed by the ammonia, which functions in the same manner as the tertiary bases in the first method for the preparation of imidosulfamide [2]. To be sure, the addition of the hydroxyl ion or of the tertiary bases proceeds much more easily then does that of the weakly basic NH_2 group of sulfamide or of ammonia, and for this reason practically quantitative yields of imidosulfamide are obtained with alkalies, while in the absence of catalysts the yields are quite minute [1].

If these schemes are correct, the substituted imidosulfamides should be obtained from all substituted sulfamides, with the exception of the tetra-substituted. This conclusion is being checked at the present time.

To synthesize other 1,5-disubstituted imidosulfamides it was necessary to obtain the monosubstituted sulfamides of type $RNHSO_2NH_2$. These compounds were obtained by Denivelle [5] and by Battegay and Meybeck [5] by a fairly complicated method, and specifically – by reacting the chlorides of the corresponding N-aryl-N-carboacylsulfamic acids with ammonia, the former being formed by the reaction of sulfuryl chloride with the sodio derivatives of N--arylcarboacylamides [6]. The monomethyl- and monoethylsulfamides were obtained by the hydrolysis of the 3--methyl- and 3-ethylimidosulfamides [3].

Paquin obtained the butyl-, cyclohexyl- and piperidylsulfamides [7] by a simpler process, and specifically – by the reaction of sulfamide with the corresponding amines.

$$RNH_2 + NH_2SO_2NH_2 \longrightarrow NH_3 + RNHSO_2NH_2 \qquad (IV)$$

Paquin makes no mention of obtaining the N-monoarylsulfamides by this scheme; for this reason it was decided to determine if it is possible to obtain N-arylsulfamides by the reaction of aromatic amines with sulfamide. It proved that the aromatic amines readily react with sulfamide when heated on the boiling water bath for several hours, but the yields of monoarylsulfamides and diarylsulfamides formed here are small, which is fully understandable, since the reaction of amines with sulfamide should give, together with the formation of substituted sulfamides, also imidosulfamide, which for all practical purposes is the solitary reaction product when sulfamide is reacted with tertiary amines [2]. In addition, the already formed N-arylsulfamide on heating and reaction with excess ammonia should give the corresponding 1,5-diarylimidosulfamide. Consequently it is impossible to decide at the present time whether the N-arylsulfamides are formed directly from amines and sulfamide by the total scheme (IV) or only as the hydrolysis products of the 1,5-diarylsulfamide found in the reaction mixture according to scheme (III).

EXPERIMENTAL

1,1,5,5-Tetramethylimidosulfamide (I). 0.05 g-mole of 1,1-dimethylsulfamide was added in one portion to 49 ml of vigorously boiling 0.5 N sodium hydroxide solution, contained in an open flask, and the boiling was continued for 10 minutes. Then the solution was cooled rapidly and evaporated to dryness in vacuo on the water bath at 30-35°. The residue, a mass of fine needle crystals, was treated with 5 ml of ethyl alcohol and after good stirring the sodium salt of (I) was suction-filtered, washed with alcohol (3 times with 1-ml portions), and dried in vacuo over sulfuric acid. The sodium salt of (I) is a colorless finely crystalline powder, readily soluble in water, difficultly soluble in alcohol, and insoluble in benzene and ether; yield 88.5%; m.p. 148-150°.

Found %: N 16.33. $C_4H_{12}O_4N_3S_2Na$. Calculated %: N 16.59.

To obtain the free (I), a solution of 0.02 g-mole of the sodium salt of (I) in 5 ml of water, cooled to 0°, was treated under stirring with 1.8 ml of 10 N sulfuric acid solution, also cooled to 0°, and 0.006 g-mole of finely pulverized sulfamic acid. The solution was evaporated in vacuo at 20° to dryness, with the receiver cooled to –20°. The dry crystalline residue was treated with 15 ml of dry acetone, the solution was vacuum-filtered, and the precipitate was washed with acetone (4 times with 5-ml portions). The filtrate was evaporated in vacuo at 20°, and the dry residue was extracted (to remove sulfamic acid) with dry ethyl acetate (2 times with 40-ml portions).

The solution was suction-filtered, the precipitate was washed with ethyl acetate (4 times with 4-ml portions), and the solution was evaporated to dryness in vacuo at 20°. The residue contained (I) as compact colorless prisms; yield 90.9%. After recrystallization from benzene, m.p. 131-133°. (I) is readily soluble in acetone, water and alcohol, somewhat more difficultly soluble in ethyl acetate, and can be recrystallized from benzene. Its water solutions show acid to Congo.

Found %: N 18.09. $C_4H_{13}O_4N_3S_2$. Calculated %: N 18.17.

1,5-Diphenylimidosulfamide (II). This compound was obtained in the same manner as (I). The sodium salt of (II) is a colorless finely crystalline powder, m.p. 206-208°; it is readily soluble in water, very difficultly soluble in alcohol, and insoluble in benzene and ether; yield 90%.

Found %: N 12.20. $C_{12}H_{12}O_4N_3S_2Na$. Calculated %: N 12.03.

The free (II) crystallizes as fine colorless prisms, soluble in benzene, acetone, alcohol and water, and with m.p. 163-165°; yield 87.1%. Its water solutions show acid to Congo.

Found %: N 13.00. $C_{12}H_{13}O_4N_3S_2$. Calculated %: N 12.84.

Hydrolysis of 1,1,5,5-Tetramethylimidosulfamide and 1,5-Diphenylimidosulfamide. A solution of 1 g of (I) in 50 ml of water was boiled for 3 minutes, and after cooling, the solution was extracted 3 times with ether (100, 50 and 50 ml). Removal of the ether by distillation left 1,1-dimethylsulfamide; yield 0.20 g; after recrystallization from benzene, m.p. 94-95°. The compound was identified by its nitrogen content and by mixed melting point.

Properties of Arylsulfamides With Formula $ArNHSO_2NH_2$

Ar	Yield (in %)	Melting point	Crystalline form	Found N (in %)	Empirical formula	Calculated N (in %)
o-$CH_3C_6H_4$	4.6	101-103°	Silvery scales	15.32	$C_7H_{10}O_2N_2S$	15.04
m-$CH_3C_6H_4$	11.8	76-78	Fine needles	14.88	$C_7H_{10}O_2N_2S$	15.04
p-$CH_3C_6H_4$	28.0	123-125	Fine needles	15.21	$C_7H_{10}O_2N_2S$	15.04
o-$CH_3OC_6H_4$	4.9	108-110	Fine prisms	13.99	$C_7H_{10}O_3N_2S$	13.85
p-$C_2H_5OC_6H_4$	4.6	125-126	Long colorless needles	13.15	$C_8H_{12}O_3N_2S$	12.96
m-$NO_2C_6H_4$	9.2	149-150	Prisms	19.49	$C_6H_7O_4N_3S$	19.35
α-$C_{10}H_7$	10.8	129-130	Fine crystalline powder	12.60	$C_{10}H_{10}O_2N_2S$	12.61
β-$C_{10}H_7$	21.1	140-142	Fine crystalline powder	12.80	$C_{10}H_{10}O_2N_2S$	12.61

Also from 1 g of (II) we obtained 0.23 g of phenylsulfamide (m.p. 105-107°); this compound was also identified by its nitrogen content and mixed melting point.

Phenylsulfamide (V). A mixture of 0.05 g-mole of sulfamide and 0.25 g-mole of aniline was heated on the boiling water bath in a flask fitted with a reflux air-condenser; here the liquid gradually separated into layers. Ammonia was slowly evolved. The cooled reaction mixture was treated with 75 ml of 1 N sodium hydroxide solution and 100 ml of ether, and the mixture shaken vigorously. The water solution was separated and then treated with concentrated hydrochloric acid until acid to Congo. Here the diphenylsulfamide deposited as a fine crystalline precipitate, while the phenylsulfamide remained in the water solution. The diphenylsulfamide (VI) was suction-filtered and washed with water (5 times with 5-ml portions), while (V) was extracted from the water solution with ether (5 times with 50-ml portions). The ether extracts were dried over sodium sulfate and the ether was distilled off. The residue contained (V), which was recrystallized from benzene; m.p. 105-107°; colorless lustrous scales. Readily soluble in water, alcohol, acetone and ether.

Found %: N 10.24. $C_6H_8N_2S$. Calculated %: N 10.46.

When the reaction mixture was heated for 2 hours the yield of (V) was 25%, and that of (VI) was 3.8%; when heated for 4 hours, the yield of (V) was 36.4% and that of (VI) was 5.8%; when heated for 6 hours, the yield of (V) was 24.1% and that of (VI) was 5.2%.

The other arylsulfamides (see Table) are obtained in similar manner.

All of the obtained arylsulfamides are readily soluble in acetone, water, alcohol and ether, with the exception

of the naphthylsulfamides, which are much more difficultly soluble in water. All of the arylsulfamides were recrystallized from benzene.

SUMMARY

The 1,5-diphenyl- and 1,1,5,5-tetramethylimidosulfamides were synthesized. It was shown that the earlier proposed scheme for the formation of imidosulfamides is incorrect, and a new scheme was proposed. A number of monoarylsulfamides were synthesized.

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TRICHLOROPHOSPHAZOARYLOXYDICHLOROACETYLS

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Recently it was found that the aliphatic esters of oxamic acid react with phosphorus pentachloride, first forming the amides of alkoxydichloroacetic acids [1] according to scheme (I), and then trichlorophosphazoalkoxydichloroacetyls [2] according to scheme (II):

$$ROCOCONH_2 + PCl_5 \longrightarrow POCl_3 + ROCCl_2CONH_2 \quad (I)$$

$$ROCCl_2CONH_2 + PCl_5 \longrightarrow 2HCl + ROCCl_2CON{=}PCl_3 \quad (II)$$

For the aromatic esters of oxamic acid [3] it has been impossible up to now to limit the reaction to scheme (I). Even in the presence of a large excess of the corresponding oxamic acid ester the reaction either does not go, or proceeds immediately according to scheme (III) with the formation of trichlorophosphazoaryloxydichloroacetyls.

$$ArOCOCONH_2 + 2PCl_5 \longrightarrow 2HCl + POCl_3 + ArOCCl_2CON{=}PCl_3 \quad (III)$$

For a possible explanation of this phenomenon see [1].

Under suitable conditions the reaction according to scheme (III) goes either quantitatively or almost quantitatively with the formation of colorless crystals of the trichlorophosphazoaryloxydichloroacetyls (IV). As a rule, the "crude" products melt only several degrees below the recrystallized material, and are usually colorless. Only in the case of the naphthoxy derivatives (XI and XII) are the crude products obtained colored and melt considerably below the pure compounds.

In their physical and chemical properties the (IV) compounds are similar to the trichlorophosphazoalkoxydichloroacetyls [2]. They react violently with water, alcohols, phenols, ammonia, amines and other substances containing active hydrogen atoms. When treated with steam, or even better, with formic acid, the (IV) compounds give in good yields the dichlorides of aryloxydichloroacetamidophosphoric acids (V) according to the scheme

$$ArOCCl_2CON{=}PCl_3 + HCOOH \longrightarrow CO + HCl + ArOCCl_2CONHPOCl_2$$

However, in contrast to the trichlorophosphazoalkoxyacetyls, the (IV) compounds are decomposed with much greater difficulty by heat. When heated they do not cleave chlorobenzene and slowly cleave phosphorus oxychloride with much greater difficulty (only at 180°). The (V) compounds are colorless crystalline compounds that melt considerably above the corresponding trichlorophosphazoaryloxydichloroacetyls (IV), and are more difficultly soluble in the common organic solvents than (IV). The (V) compounds react slowly with water at room temperature, and consequently they can be stored without taking any special precautions. When heated with water the (V) compounds are rapidly hydrolyzed, and they react vigorously with compounds containing active hydrogen atoms.

EXPERIMENTAL

All of the solvents and starting substances were carefully dehydrated. All of the operations were run in such manner that both the reaction mixtures and reaction products were exposed to atmospheric moisture as little as possible.

Trichlorophosphazophenoxydichloroacetyl (VI). A mixture of 0.025 g-mole of pulverized phenyl oxamate and 0.05 g-mole of finely divided phosphorus pentachloride was thoroughly mixed in a round-bottomed flask, closed with reflux condenser, which was connected to a gas bubbler containing sulfuric acid and a water trap for collecting hydrogen chloride. The evolution of hydrogen chloride began in 1 to 2 minutes. The flask contents

became completely liquid within 10 minutes. The reaction was accompanied by the absorption of heat. In 15--20 minutes, when the evolution of hydrogen chloride had slackened considerably, the flask was immersed in a water bath, heated to 40°. The reaction was ended within 30 minutes. The reaction mixture was cooled and the hydrogen chloride was displaced by dry air. The yield of mixed phosphorus oxychloride and (VI) was quantitative, while the yield of hydrogen chloride was 92%. The phosphorus oxychloride was vacuum-distilled (5 mm) at 20-30° into a receiver cooled to −21°; yield 97%. The residue was crude (VI) as a light yellow turbid liquid; yield 101%. The crude product soon crystallized; m.p. 45° (last crystal, bulb of the thermometer in the liquid). Recrystallization from 10 ml of petroleum ether (b.p. 85-95°) gave the compound as colorless prisms (m.p. 49-50°).

Found %: N 4.00; Cl 49.50, 49.44. Equiv. after hydrolysis 8.13, 8.04. $C_8H_5O_2NPCl_5$. Calculated %: N 3.94; Cl 49.97. Equiv. after hydrolysis 8.00.

The following compounds were obtained in similar manner.

Trichlorophosphazo-o-cresoxydichloroacetyl (VII). The crude product melts at 46° (last crystal). Recrystallization from petroleum ether (85-95°; 2 ml per 0.01 g-mole) gave the compound as coarse colorless prisms (m.p. 49-51°); yield 64%.

Found %: Cl 47.89; P 8.75. Equiv. after hydrolysis 8.02, 8.10. $C_9H_7O_2NPCl_5$. Calculated %: Cl 48.00; P 8.38. Equiv. after hydrolysis 8.00.

Trichlorophosphazo-m-cresoxydichloroacetyl (VIII). The crude product can be recrystallized from a very small volume of petroleum ether (85-95°). Cooling the solution to −10° gave (VIII) as clusters of transparent needles; m.p. 30-34°.

Found %: Cl 47.96, 48.19; P 8.43. Equiv. after hydrolysis 7.99, 7.99. $C_9H_7O_2NPCl_5$. Calculated %: Cl 48.0; P 8.38. Equiv. after hydrolysis 8.00.

Trichlorophosphazo-p-cresoxydichloroacetyl (IX). Crude (IX) melts at 76° (last crystal). Recrystallization from petroleum ether (1 ml per g of compound) gave the compound as long colorless needles (up to 5 mm); m.p. 74-76°.

Found %: N 3.86; Cl 47.86, 47.98; P 8.28. Equiv. after hydrolysis 8.12, 8.18. $C_9H_7O_2NPCl_5$. Calculated %: N 3.79; Cl 48.00; P 8.38. Equiv. after hydrolysis 8.00.

Trichlorophosphazo-p-chlorophenoxydichloroacetyl (X). The reaction was run at 60-75° for 20-25 minutes. Crude (X) melts at 55° (last crystal); recrystallization from petroleum ether (1 ml per 0.01 g-mole) gave the compound as colorless transparent prisms (m.p. 52-55°).

Found %: hydrolyzable Cl 45.57, 45.62; P 8.32. Equiv. after hydrolysis 8.19, 8.22. $C_8H_4O_2NPCl_6$. Calculated %: hydrolyzable Cl 45.48; P 7.95. Equiv. after hydrolysis 8.00.

Trichlorophosphazo-α-naphthoxydichloroacetyl (XI). The reaction was run at 45° for 1 hour. The crude (XI) had a brown color; m.p. 45° (last crystal). After two recrystallizations from either petroleum ether (using each time 8 ml of solvent per 0.01 g-mole of compound) or carbon tetrachloride (0.5 ml per g of substance) the compound was obtained as fine colorless prisms (m.p. 69-72°).

Found %: Cl 43.78; 44.09; P 7.71. Equiv. after hydrolysis 8.22, 8.06. $C_{12}H_7O_2NPCl_5$. Calculated %: Cl 43.74; P 7.64. Equiv. after hydrolysis 8.00.

Trichlorophosphazo-β-naphthoxydichloroacetyl (XII). The reaction was run at 45° for 1 hour. The crude (XII) was colored a light crimson; m.p. 78° (last crystal). Recrystallization from petroleum ether (10 ml per 4 g of substance) gave the compound as colorless needles (m.p. 80-83°); yield 64%.

Found %: Cl 44.06, 44.20; P 7.95. Equiv. after hydrolysis 8.28, 8.20. $C_{12}H_7O_2NPCl_5$. Calculated %: Cl 43.74; P 7.68. Equiv. after hydrolysis 8.00.

All of the (IV) compounds are readily soluble at 20° in acetone, ether and benzene. (VI), (VIII), (IX) and (X) are readily soluble in carbon tetrachloride, while (VII), (XI) and (XII) are difficultly soluble. All of the (IV) compounds are slightly soluble [(X) is somewhat more soluble] in petroleum ether (85-95°) at 20°, while on heating, (XI) and (XII) are readily soluble, and (VI)-(X) are very soluble.

Phenoxydichloroacetamidophosphoryl Dichloride (XIII). To a solution of 0.01 g-mole of (VI) in 15 ml of

benzene was added 0.01 g-mole of anhydrous formic acid. A vigorous reaction began immediately with the evolution of hydrogen chloride and carbon monoxide, and (XIII) was deposited as a fine crystalline precipitate, which was suction-filtered, washed with benzene, dried in vacuo, and recrystallized from either 10 ml of petroleum ether (85-95°) or 10 ml of carbon tetrachloride. (XIII) was obtained as colorless transparent prisms; m.p. 155-156°; yield 96%; readily soluble at 20° in dioxan and acetone, and when heated it is soluble in ether, chloroform, dichloroethane, benzene, toluene, carbon tetrachloride and petroleum ether.

Found %: N 4.29; Cl 42.01, 41.97. Equiv. after hydrolysis 7.03, 7.00. $C_8H_6O_3NPCl_4$. Calculated %: N 4.16; Cl 42.09. Equiv. after hydrolysis 7.00.

The following compounds were obtained in similar manner.

o-Cresoxydichloroacetamidophosphoryl Dichloride (XIV). Yield 88%, colorless needles (from benzene); m.p. 128-130°.

Found %: Cl 40.34, 40.24; P 9.57. Equiv. after hydrolysis 7.07, 7.07. $C_9H_8O_3NPCl_4$. Calculated %: Cl 40.42; P 9.06. Equiv. after hydrolysis 7.00.

m-Cresoxydichloroacetamidophosphoryl Dichloride (XV). Yield 61%, fine needles (from benzene); m.p. 161-163°.

Found %: Cl 40.19, 40.29; P 9.00. Equiv. after hydrolysis 7.08, 7.11. $C_9H_8O_3NPCl_4$. Calculated %: Cl 40.42; P 9.06. Equiv. after hydrolysis 7.00.

p-Cresoxydichloroacetamidophosphoryl Dichloride (XVI). Yield 98%, slender colorless needles (from benzene); m.p. 144-146°.

Found %: N 3.95; Cl 40.37, 40.38; P 9.12. Equiv. after hydrolysis 7.09, 7.08. $C_9H_8O_3NPCl_4$. Calculated %: N 3.99; Cl 40.42; P 9.06. Equiv. after hydrolysis 7.00.

α-Naphthoxydichloroacetamidophosphoryl Dichloride (XVII). Yield 34%, aggregates of needles resembling snowflakes (from benzene); m.p. 140-142°.

Found %: Cl 36.56; P 8.00. Equiv. after hydrolysis 7.06, 7.03. $C_{12}H_8O_3NPCl_4$. Calculated %: Cl 36.67; P 8.01. Equiv. after hydrolysis 7.00.

β-Naphthoxydichloroacetamidophosphoryl Dichloride (XVIII). Yield 60%, colorless needles (from benzene); m.p. 163-165°.

All of the (V) compounds are readily soluble in acetone, difficultly soluble in cold benzene, and readily soluble in boiling benzene. (XVI) is readily soluble in ether, (XIV), (XVII) and (XVIII) are difficultly soluble, and (XV) is very difficultly soluble. (XIV)-(XVI) are difficultly soluble in carbon tetrachloride and petroleum, while (XVII) and (XVIII) are very difficultly soluble.

SUMMARY

Some trichlorophosphazoaryloxydichloroacetyls and dichlorides of aryloxydichloroacetamidophosphoric acids were synthesized.

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REACTION OF TETRAFLUOROETHYLENE WITH ARSENIC TRICHLORIDE IN THE PRESENCE OF ALUMINUM CHLORIDE

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In recent years the reaction of tetrafluoroethylene with a whole series of different compounds has been accomplished: with halides, hydrogen halides, sulfur chloride, nitrogen dioxide, ammonia, amines, alcohols, glycols, alkyl halides, mercaptans, hydroxy mercaptans, ethylene, acrolein, acrylonitrile, vinyl chloride, etc. [1]. Despite the large number of reactions described, up to now only a very few examples are known of the reaction of tetrafluoroethylene with metal halides and the preparation of perfluoroorganometallic compounds.

The reaction of arsenic trichloride with tetrafluoroethylene wasstudied in the present paper. The reaction of arsenic trichloride with unsaturated compounds has been extensively studied only in the case of reaction with acetylene [2-7]. The reaction with ethylene has been studied to a lesser degree. Renshaw and Ware [8] and the Nekrasovs [9] have shown that the saturation of arsenic trichloride with ethylene in the presence of anhydrous aluminum chloride at atmospheric pressure and room temperature results in the formation of β-chloroethyldichloroarsine in low yield.

We first attempted to react tetrafluoroethylene with arsenic trichloride under conditions similar to those used in the reaction with ethylene, i.e., by saturating arsenic trichloride with tetrafluoroethylene in the presence of aluminum chloride at atmospheric pressure. The results were negative: we were unable to isolate any organoarsenic compounds here. Equally unsuccessful were the experiments run in an autoclave under pressure, but without the aluminum chloride. On making a more detailed study of this reaction it was established by us that when arsenic trichloride is reacted with tetrafluoroethylene in the presence of aluminum chloride in a rotating autoclave at 70--90° for 9-12 hours the main product in the obtained reaction mixture is a substance containing carbon, fluorine, chlorine and arsenic. Based on the analysis data, molecular weight and molecular refraction, and also based on the analysis of the transformation and decomposition products, the substance was identified as being the previously unknown pentafluoroethyldichloroarsine. The substance is a colorless liquid with b.p. 86-87°, with the sharp odor characteristic of arsine chlorides. Besides pentafluoroethyldichloroarsine, we isolated a second substance from the reaction mixture – a colorless liquid with b.p. 20-21°. This substance decolorized bromine water; based on the analysis data, molecular weight and boiling point, and also based on the physicochemical properties of the bromide obtained from it, this substance corresponds to the known 1,1-difluoro-2,2-dichloroethylene [10].

The described reaction can be depicted by the following scheme.

$$3CF_2=CF_2+2AsCl_3 \xrightarrow{AlCl_3} 2CF_3CF_2AsCl_2+CF_2=CCl_2 \qquad (1)$$

The yield of pentafluoroethyldichloroarsine based on reacted arsenic trichloride was 70%, and based on tetrafluoroethylene taken for reaction it was 50-60% of the theoretical [in accordance with equation (1)].

The formation of pentafluoroethyldichloroarsine as the result of Reaction (1), instead of the expected tetrafluoro-β-chloroethyldichloroarsine, indicated that this process is different from the usual reaction for the addition of arsenic trichloride to unsaturated compounds. The explanation for this peculiar behavior should be sought in the ability shown by aluminum chloride to exchange its chlorine for fluorine when reacted with fluorinated hydrocarbons [11-15]. It seems probable that also in the discussed case the first reaction to take place is exchange of halogen between tetrafluoroethylene and aluminum chloride.

$$CF_2=CF_2+AlCl_3 \rightarrow AlF_2Cl+CF_2=CCl_2 \qquad (2)$$

Evidence in support of this is the fact that in all of the experiments the amount of difluorodichloroethylene isolated, together with pentafluoroethyldichloroarsine, corresponded to the ratio shown by Equation (1). Subsequent reaction of the tetrafluoroethylene with arsenic trichloride and aluminum difluorochloride results in the formation of pentafluoroethyldichloroarsine and aluminum fluorodichloride, both of which are present in the reaction mixture.

$$CF_2=CF_2 + AlF_2Cl + AsCl_3 \xrightarrow{AlCl_3} CF_3CF_2AsCl_2 + AlFCl_2 \quad (3)$$

The aluminum fluorodichloride formed in this manner can also react with tetrafluoroethylene, again yielding aluminum difluorochloride.

$$CF_2=CF_2 + 2AlFCl_2 \longrightarrow CF_2=CCl_2 + 2AlF_2Cl \quad (4)$$

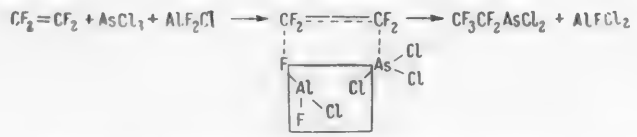
The presented schemes satisfactorily explain the fact that comparatively small amounts of aluminum chloride are sufficient for the transformation of substantial amounts of tetrafluoroethylene to pentafluoroethyldichloroarsine and difluorodichloroethylene (see Table).

Reaction of Tetrafluoroethylene With Arsenic Trichloride in the Presence of Aluminum Chloride

Change (in g)			Temperature (in autoclave)	Reaction time (in hours)	Weight of obtained reaction mass (in g)	Fractions isolated (in g)		Analysis of $C_2F_5AsCl_2$ (in %)		Yield based on $CF_2=CF_2$ (in % of theoretical)*	
$AsCl_3$	$AlCl_3$	$CF_2=CF_2$				b.p. 20–21°	b.p. 86–87°	As	Cl	$C_2F_5AsCl_2$	C_2F_5Cl
365	8.8	44	70—80°	18	386.5	11.7	34.5	27.25	26.35	44.4	60.6
252.2	8.1	24	70	9	254.5	6.2	20.5	26.4	25.8	48.3	59.0
253.1	9.4	22	70	9	274.8	6.7	20.4	27.0	27.0	52.5	69.7
142.5	7.1	13	90—125	12	159.9	3.7	11.3	25.8	25.0	49.3	64.9
254	9.0	73.6	50—70	21	300	19.3	56.1	26.6	25.8	43.3	59.0
255	5.75	20	80—100	40	267.1	6.0	18.0	26.05	24.7	50.9	68.0

*The yield was calculated according to Equation (1) without considering the pentafluoroethyldichloroarsine contained in the intermediate fractions.

The described process can be depicted by the following general scheme, postulating the formation of an intermediate complex, the decomposition of which leads to the formation of pentafluoroethyldichloroarsine and aluminum fluorodichloride.



The presence of 1,1-difluoro-2,2-dichloroethylene in the reaction mixture in amounts corresponding to Equation (1) indicates that under the described conditions this compound is practically inert toward arsenic trichloride, present in excess. This is also supported by the fact that we were unable to find any other organoarsenic compounds besides pentafluoroethyldichloroarsine in the reaction products.

A study of the properties of the obtained pentafluoroethyldichloroarsine revealed that this compound is easily decomposed by aqueous alkali solutions in the cold with a nearly quantitative evolution of pentafluoroethane, which is additional evidence that this compound has the structure of pentafluoroethyldichloroarsine. The oxidation of pentafluoroethyldichloroarsine with hydrogen peroxide in the cold gave pentafluoroethylarsonic acid. The silver salt of the acid was obtained as white scales with a mother-of-pearl luster. The reduction of pentafluoroethylarsonic acid with sulfur dioxide in hydrochloric acid medium gave pentafluoroethyldichloroarsine, identical with the product isolated in the reaction of tetrafluoroethylene with arsenic trichloride. The heating of pentafluoro-

ethyldichloroarsine with ammonium fluoride at 70° gave pentafluoroethyldifluoroarsine as a colorless liquid, boiling at 47-48°, and having a sharp odor. The reduction of pentafluoroethyldichloroarsine with zinc in alcohol-hydrochloric acid medium gave pentafluoroethylarsine, obtained as a colorless transparent liquid with b.p. 27-28°.

EXPERIMENTAL

1. Reaction of Tetrafluoroethylene With Arsenic Trichloride in the Presence of Aluminum Chloride. Into a 500-ml, rotated, stainless steel autoclave, fitted with thermocouple well, valve, manometer and safety disc, was charged 250-300 g of freshly distilled arsenic trichloride and 7-9 g of freshly sublimed aluminum chloride. After this the air was removed from the autoclave by means of a vacuum-pump to a vacuum of 4-5 mm. To remove the last traces of air the autoclave was blown with tetrafluoroethylene and then filled with the same gas to a pressure of 9-14 atm., which corresponded to 16-30 g of C_2F_4. During the first 5 hours the autoclave was rotated without heating, and then the electrical heat was turned on; the temperature in the autoclave was gradually raised to 70-90°. The autoclave was rotated at this temperature for 9-12 hours. The pressure at the end of reaction usually dropped to atmospheric.

The reaction mass unloaded from the autoclave was fractionally distilled. After 2-3 distillations in a CO_2 atmosphere we isolated, besides unreacted arsenic trichloride, two fractions:

1st Fraction with b.p. 20-21° was 1,1-difluoro-2,2-dichloroethylene.

Found M 138. $C_2F_2Cl_2$. Calculated M 133.

Bromination of the obtained difluorodichloroethylene gave the dibromide with b.p. 138-139° and m.p. 45°, corresponding to 1,1-difluoro-2,2-dichloro-1,2-dibromoethane (according to the literature data [10]: b.p. 138.8-139°, m.p. 45.5°).

Found %: F 12.0; Cl + Br (calculated as Cl) 48.3. $C_2F_2Cl_2Br_2$. Calculated %: F 12.9; Cl + Br 48.4.

2nd Fraction with b.p. 86-87° was a colorless transparent liquid with a sharp odor, and was pentafluoroethyldichloroarsine.

d^{20}_4 1.9221, $n^{20}D$ 1.4063, MR_D 33.56; calc. 33.56.

Found %: As 28.8; Cl 26.55; F 34.9; C 9.55. M 260. $C_2F_5Cl_2As$. Calculated %: As 28.3; Cl 26.7; F 35.6; C 9.0. M 265.

The distillation residue, a grayish viscous mass, was treated with concentrated hydrochloric acid. Evaporation of the solution gave a residue from which the hydrate of aluminum fluorodichloride, corresponding to the composition $AlFCl_2 \cdot 6H_2O$, was isolated.

Found %: F 7.3; Cl 32.1; Al 11.9. $AlFCl_2 \cdot 6H_2O$. Calculated %: F 8.4; Cl 31.5; Al 12.0.

The results of the experiments, run under various conditions, are given in the Table.

From the data given in the table it follows that the optimum reaction conditions are a time of 9-12 hours at 70-90° and molar ratios $AsCl_3 : C_2F_4 : AlCl_3 = 1.39 : 0.22 : 0.07$. An increase in the amount of aluminum chloride, and also the reaction time, do not affect the yield of pentafluoroethyldichloroarsine.

2. Decomposition of Pentafluoroethyldichloroarsine With Alkali Solution. A solution of potassium hydroxide (8 g of KOH in 76 ml of water) was placed in a flask, fitted with dropping funnel and connected to a trap, cooled to −80°. 10 g of pentafluoroethyldichloroarsine was added gradually from the dropping funnel. Here 4 g of a clear colorless liquid condensed in the trap, which when fractionally distilled through a Podbelniak column almost completely distilled at −49 to −49.5° (pentafluoroethane has b.p. −48.5° [16]).

Found %: C 20.9. M 122.4. C_2F_5H. Calculated %: C 20.0. M 120.0.

3. Oxidation of Pentafluoroethyldichloroarsine to Pentafluoroethylarsonic Acid. Into a 100-ml flask was charged 20.2 g of pentafluoroethyldichloroarsine and 20 ml of water. Then 26 g of aqueous hydrogen peroxide solution (14.7% H_2O_2) was added gradually at 1-2°. The water was vacuum-distilled. The residue was washed with benzene and dried at 100° to constant weight. The acid was obtained as a fine crystalline powder. The silver salt of the acid was obtained as white scales with a mother-of-pearl luster.

Found %: As 16.5; F 22.1; Ag 47.4. $C_2F_5O_3Ag_2As$. Calculated %: As 16.4; F 20.75; Ag 47.1.

4. Converstion of Pentafluoroethylarsonic Acid to Pentafluoroethyldichloroarsine. Four grams of pentafluoroethylarsonic acid was mixed with 20 ml of hydrochloric acid (1 : 1), a crystal of potassium iodide was added, and then sulfur dioxide was passed through the mixture for 30 minutes. The reaction product was separated from the aqueous layer, dried over sodium sulfate, and then distilled. We isolated 1 g of substance with b.p. 86-87°.

Found %: As 27.8; Cl 26.3. $C_2F_5Cl_2As$. Calculated %: As 28.3; Cl 26.7.

5. Preparation of Pentafluoroethyldifluoroarsine. Into a distilling flask, fitted with Vigreux column and descending condenser, was charged 5.9 g of pentafluoroethyldichloroarsine and 2.5 g of ammonium fluoride. The flask contents were heated on the water bath, the temperature of which was gradually raised to 70°; here 2 g of a clear colorless liquid with a sharp odor was obtained as distillate, which after redistillation had the following constants.

B. p. 47-48°, d^{20}_4 2.0754, $n^{20}D$ 1.3472, MR_D 23.73; calc. 23.03.

Found %: As 31.65; F (hydrolyzable) 15.8. M 232. C_2F_7As. Calculated %: As 32.3; F (hydrolyzable) 16.3. M 232.

6. Preparation of Pentafluoroethylarsine. Into a round-bottomed flask, fitted with reflux condenser and two dropping funnels, was charged 10-12 g of granulated zinc. A mixture of 50 ml of concentrated hydrochloric acid and 25 ml of methanol was placed in one dropping funnel, and a mixture of 26 g of pentafluoroethyldichloroarsine and 25 ml of methanol was placed in the other. The hydrochloric acid-alcohol mixture and the alcohol solution of pentafluoroethyldichloroarsine were added alternately to the flask with zinc. Here the flask contents became quite hot. The gases escaping from the flask, after being washed in two water towers and dried over calcium chloride, entered a trap cooled to −50°. 7.5 g of a clear colorless liquid condensed in the trap, which was distilled in a stream of CO_2; b.p. 26-27°, $n^{20}D$ 1.331.

Found %: As 37.0; F 47.9. M 208.7. $C_2H_2F_5As$. Calculated %: As 38.2; F 48.4. M 196.0.

SUMMARY

1. Tetrafluoroethylene was made to react with arsenic trichloride in the presence of aluminum chloride at elevated temperature and under pressure, and some concepts were expressed regarding the mechanism of this process. The previously unknown pentafluoroethyldichloroarsine was isolated as the main reaction product.

2. The previously unknown pentafluoroethyldifluoroarsine, pentafluoroethylarsine and pentafluoroethylarsonic acid were synthesized and characterized.

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STRUCTURE AND CHEMICAL TRANSFORMATIONS OF ALKALI-ORGANIC COMPOUNDS OF ANILS

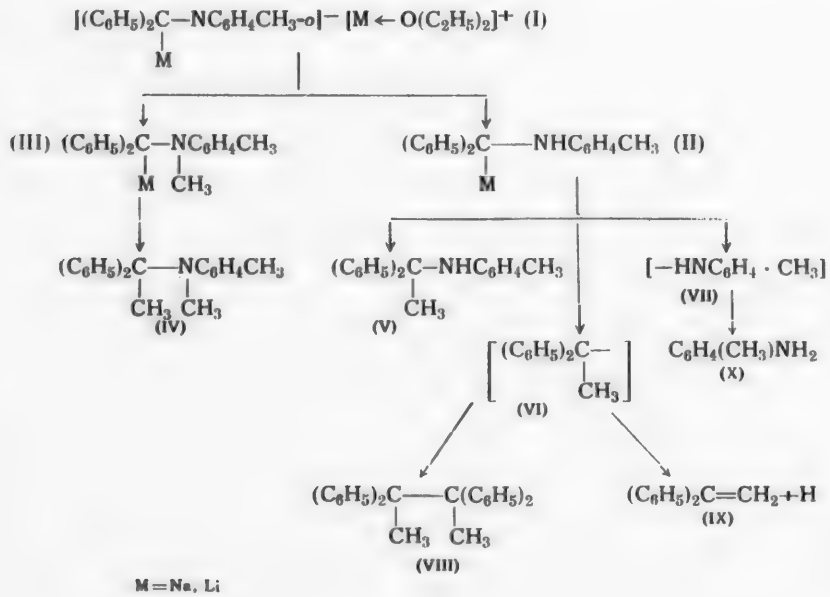
III. TRANSFORMATIONS OF DISODIUM AND DILITHIUM COMPOUNDS OF BENZOPHENONE-o-TOLYLIMIDE AND BENZOPHENONE-p-TOLYLIMIDE UNDER THE INFLUENCE OF ALKYL HALIDES

B. M. Mikhailov and K. N. Kurdiumova

In the previous communication [1] it was shown that complex transformations occur when alkyl halides are reacted with dimetallic compounds of benzophenonephenylimide. The products formed as a result of these transformations are phenylbenzhydrylamine, the product of replacing both of the atoms of the alkali metal by hydrogen atoms, and a number of substances that arise as the result of the molecules decomposing at the carbon–nitrogen bond, namely aniline, phenylated ethylenic hydrocarbons, 2,2,3,3-tetraphenylbutane (when a methyl halide is used), and also gaseous hydrocarbons.

To determine the influence exerted by the structure of the aryl radical on the nitrogen atom on the reaction course of dimetallic compounds of anils we studied the reaction of methyl chloride and iodide with the disodium and dilithium compounds of benzophenone-o-tolylimide and benzophenone-p-tolylimide $(C_6H_5)_2C{=}NC_6H_4CH_3$-(o- or p-) · $2M(C_4H_{10}O)$ (M = Na or Li).

A complex reaction is observed when the dilithium compound of benzophenone-o-tolylimide is reacted with methyl iodide, leading to the formation of various substances. The collective transformations can be depicted by the following scheme



Reaction Products of Dimetallic Compounds $(C_6H_5)_2C{=}NC_6H_4CH_3$-(o- or p-) · $2M(C_4H_{10}O)$ (From 20 g of Anil) With Alkyl Halides

Starting compounds			Obtained (in %)					Amount of gas (in ml)
dimetallic compound		alkyl halide	$(C_6H_5)_2C(CH_3)-N(CH_3)C_6H_4CH_3$ (IV)	$(C_6H_5)_2C(CH_3)-NHC_6H_4CH_3$ (V)	$C_6H_4(CH_3)NH_2$ (X)	$(C_6H_5)_2C=CH_2$ (IX)	$(C_6H_5)_2C-C(C_6H_5)_2$ (VIII)	
position of CH_3 group in tolyl radical	metal							
Ortho	Li	CH_3I	8.0	15.0	30.7	29.0	6.0	162
Ortho	Na	CH_3I	4.0	16.0	32.0	30.0	10.6	967
Para	Li	CH_3Cl	20.8	—	57.6	33.8	8.0	82
Para	Na	CH_3I	28.8	—	41.7	33.8	3.0	800

The starting dimetallic compound (I) apparently has the same structure as the dimetallic compound of benzophenone-phenylimide. In the proposed scheme it is assumed that the atoms of the metal react in sequence, in which connection the ionized atom of the metal reacts first [2]. The difference between the discussed scheme for the transformations of the dimetallic compounds of benzophenonephenylimide homologs and the scheme for the transformations of the dimetallic compounds of benzophenonephenylimide itself consists in the fact that compound (I) in the first phase of reaction is not only capable of replacing the ionized atom of the metal by hydrogen with the formation of (II), but is also capable of replacing the ionized atom by a hydrocarbon radical with the formation of a monometallic compound (III), which then exchanges the metal for a methyl group and is converted to the tertiary amine – the N-methyl-1,1-diphenylethylamine (IV).

Compound (II) does not undergo reduction, as is observed in the benzophenonephenylimide series, but instead exchanges the metal for the methyl group and in this connection partially retains the anil skeleton, being converted to N-(o-tolyl)-1,1--diphenylethylamine (V), and in part suffers decomposition at the C–N bond with the formation of radicals (VI) and (VII). Further transformations of the latter are analogous to the transformations of the radicals obtained from the dimetallic compounds of benzophenonephenylimide itself, and lead to the formation of 1,1-diphenylethylene (IX), 2,2,3,3-tetraphenylbutane (VIII) and o-toluidine (X) (see Table).

N-(o-Tolyl)-1,1-diphenylethylamine (V) and N-methyl--N-(o-tolyl)-1,1-diphenylethylamine (IV) were obtained as a mixture, for the separation of which we used a new method of separating amines, based on the metalation reaction. This method consists in selective reaction with butyllithium, where the secondary amine (V) is converted to the lithium amide and is isolated from the solution (using a suitable solvent), while the tertiary amine (IV) remains unchanged in the solution. N--(o-Tolyl)-1,1-diphenylethylamine (V) was identified by comparing it with the synthetic specimen, obtained by the addition of phenyllithium to acetophenone-o-tolylimide and subsequent hydrolysis of the lithium derivative.

$$C_6H_5C(CH_3){=}NC_6H_4CH_3 + C_6H_5Li \rightarrow$$

$$\rightarrow (C_6H_5)_2C(CH_3)-NC_6H_4CH_3(Li) \rightarrow (C_6H_5)_2C(CH_3)-NHC_6H_4CH_3$$

The behavior of the disodium compound of benzophenone--o-tolylimide toward methyl iodide is similar to that of the dilithium compound, with the only difference that a large amount of gaseous products is obtained (see Table).

Next we investigated the reaction between dilithium benzophenone-p-tolylimide and methyl chloride. Using the above described method of analyzing the reaction products, it was established that when dilithium benzophenone-

-p-tolylimide is reacted with methyl chloride, of the compounds retaining the skeleton of the original molecule, only the tertiary amine – N-methyl-N-(p-tolyl)-1,1-diphenylethylamine – is formed. Besides this compound, the other products formed during reaction are p-toluidine, 1,1-diphenylethylene and 2,2,3,3-tetraphenylbutane (see Table). The amount of gaseous products obtained was small. The reaction between disodium benzophenone-p--tolylimide and methyl iodide proceeds in a similar manner. The same compounds are obtained as with methyl chloride, but in somewhat different proportions.

The transformations of the dimetallic compounds of benzophenone-p-tolylimide can be depicted by the above described scheme with the difference that in this case the compound, corresponding to compound (V), is not obtained, while the monometallic compound of type (II), exchanging the metal for the methyl group, suffers only decomposition at the C–N bond with the formation of 1,1-diphenylethyl radicals (IV) and a radical similar to (VII).

EXPERIMENTAL

The dimetallic compounds of benzophenone-o-tolylimide and benzophenone-p-tolylimide were obtained using the conditions described for the preparation of the organometallic compounds of benzophenonephenylimide [1].

Reaction of Dilithium Benzophenone-o-tolylimide With Methyl Iodide. The reaction between methyl iodide (11.4 g) and dilithium benzophenone-o-tolylimide, obtained from 20 g (0.07 g-mole) of anil and 1.62 g (0.23 g--atom) of lithium in 200 ml of absolute ether, was run under the conditions described earlier for the reaction of disodium benzophenonephenylimide with methyl iodide [2]. The compounds obtained from the reaction are described below.

1. N-Methyl-N-(o-tolyl)-1,1-diphenylethylamine and N-(o-tolyl)-1,1-diphenylethylamine were isolated as a water-insoluble mixture of amine hydrochlorides (5.45 g). The hydrochlorides of the amines were converted to the free base by treatment with 10% alcoholic NaOH solution. The obtained oily product was vacuum-distilled at 192-212° (10 mm) to give a viscous yellow oil, which partially crystallized on standing. To separate the secondary and tertiary amines, 1 g of the oily product with b.p. 195-212° (10 mm) was dissolved in 50 ml of petroleum ether; the solution was placed in a Dewar ampul, and then treated with a solution of butyllithium in petroleum ether (6 ml, 0.01 mole). The resulting precipitate of lithium amide was filtered on a special filter in a nitrogen atmosphere and then vacuum-dried. We obtained 0.65 g of the lithium amide, which after treatment with methanol gave 0.5 g of substance with m.p. 96-99°, after recrystallization from methanol having m.p. 99.5-101°.

Found %: C 87.76; H 7.49. $C_{21}H_{21}N$. Calculated %: C 87.76; H 7.40.

The substance does not depress the melting point when mixed with a specimen of the N-(o-tolyl)-1,1-diphenylethylamine obtained from acetophenone-o-tolylimide and phenyllithium.

The filtrate after removal of the lithium amide was worked up to yield 0.35 g of an oily substance, which crystallized on standing. After recrystallization from methanol the substance had m.p. 110-112° and was the tertiary amine – N-methyl-N-(o-tolyl)-1,1-diphenylethylamine (IV).

Found %: C 87.44; H 7.53. $C_{22}H_{23}N$. Calculated %: C 87.66; H 7.69.

The hydrochloride of N-methyl-N-(o-tolyl)-1,1-phenylethylamine crystallizes from acetone as slender needles, m.p. 215-216°.

2) o-Toluidine. The hydrochloric acid solution, obtained after treating the reaction products with hydrochloric acid, was made alkaline, and the oil extracted with benzene and then distilled. We obtained 2.4 g (30%) of o-toluidine, b.p. 62-63° (2 mm), d^{20}_4 0.9936, $n^{20}D$ 1.5686.

3) 1,1-Diphenylethylene. The benzene extract, obtained after treating the reaction products with hydrochloric acid, was evaporated and the residue was fractionated. We obtained 3.8 g (29.0%) of 1,1-diphenylethylene with b.p. 102-105° (2 mm), $n^{20}D$ 1.6084.

4. 2,2,3,3-Tetraphenylbutane. The residue from the distillation of the 1,1-diphenylethylene in an amount of 2.8 g was chromatographed on aluminum oxide. Petroleum ether was used for the elution. We obtained 0.8 g of substance with m.p. 126-127°. Yield of 2,2,3,3-tetraphenylbutane was 6%.

In this experiment we obtained 162 ml of gas with the following composition (in %): acetylene 3.88, propylene + + butylene 1.48, ethylene 4.44, hydrogen 4.63, higher hydrocarbons 4.63, methane 80.9.

Acetophenone-o-tolylimide. A mixture of 18 g (0.5 g-mole) of acetophenone acetal [3] and 10.7 g (1 g--mole) of o-toluidine was boiled under reflux for 45 minutes, and then the reaction product was distilled at 157-159° (6 mm). We obtained 8.08 g of acetophenone-o-tolylimide, which after recrystallization from petroleum ether and ethanol had m.p. 59-60°, which agrees with the literature [4]. The yield of the anil was 40%.

N-(o-Tolyl)-1,1-diphenylethylamine (from acetophenone-o-tolylimide and phenyllithium). A solution of 7.0 g (0.03 g-mole) of acetophenone-o-tolylimide in 30 ml of absolute ether was placed in a nitrogen-filled Dewar ampul, and then an ether solution of phenyllithium (43.3 ml of an 0.116 N solution) was added. The ampul was sealed and heated for 3 hours at 35-40°. Then the reaction mass was treated with methanol and water. The residue, obtained from the ether solution, was vacuum-distilled. We obtained 2.4 g of a viscous yellow oil with b.p. 200-210° (7 mm), which immediately crystallized when rubbed with petroleum ether, m.p. 99-101°. Recrystallization from methanol gave the compound as colorless prisms, m.p. 99.5-101°.

Found %: C 87.56; H 7.36. $C_{21}H_{21}N$. Calculated %: C 87.76; H 7.40.

SUMMARY

1. The presence and position of a methyl group in the aryl radical on the nitrogen atom of the azomethine bond exerts substantial influence on the reaction course when methyl halides are reacted with the dimetallic derivatives of benzophenone-o-tolylimide and benzophenone-p-tolylimide.

2. The dimetallic derivatives of benzophenone-o-tolylimide when reacted with methyl iodide are capable of replacing the atoms of the metal by methyl groups with the formation of the secondary amine — N-(o-tolyl)--1,1-diphenylethylamine — and the tertiary amine — N-methyl-N-(o-tolyl)-1,1-diphenylethylamine. Simultaneously with the formation of the amines, cleavage of the azomethine bond in the dimetallic derivative is observed and the formation of o-toluidine, 1,1-diphenylethylene and 2,2,3,-tetraphenylbutane.

3. The reaction of a methyl halide with the dimetallic derivatives of benzophenone-p-tolylimide proceeds with the simultaneous formation of the tertiary amine — N-methyl-N-(p-tolyl)-1,1-diphenylethylamine — and the cleavage of the C—N bond in the dimetallic compound with the formation of p-toluidine, 1,1-diphenylethylene and 2,2,3,3-tetraphenylbutane.

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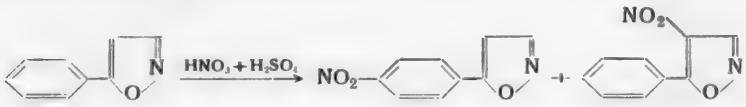
ISOXAZOLE DERIVATIVES

V. SUBSTITUTION IN 5-PHENYLISOXAZOLE

N. K. Kochetkov and E. D. Khomutova

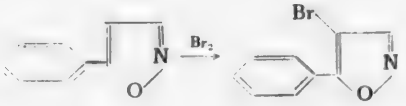
Although oxazole derivatives were discovered in 1888, relatively few members of this class of compounds are known. It is known that individual members of this class of compounds can be nitrated [1], halogenated [2], and sulfonated [3]. However, the position held by isoxazole in the aromatic series of compounds has not been established up to now. The activity of the isoxazole nucleus in substitution reactions when compared with other aromatic systems has also not been investigated. We undertook a study of the activity of the isoxazole nucleus in electrophilic substitution reactions, such as nitration and halogenation, and also in the mercuration reaction. It seemed of interest to determine the activity of the isoxazole nucleus in comparison, for example, to the benzene ring. As the first example we chose the earlier slightly studied 5-phenylisoxazole.

5-Phenylisoxazole was synthesized by the earlier described method [4] from phenyl β-diethylaminovinyl ketone and hydroxylamine hydrochloride in methanol. The nitration of 5-phenylisoxazole with a mixture of nitric and sulfuric acids under cooling gave in a total yield of 75% a mixture of nitro products, which contained 45% of 5-(p-nitrophenyl)isoxazole, identical with the substance obtained from p-nitrophenyl β-chlorovinyl ketone and hydroxylamine hydrochloride [4], and 30% of a nitro-5-phenyloxazole, the oxidation of which with potassium permanganate resulted in the isolation of benzoic acid.



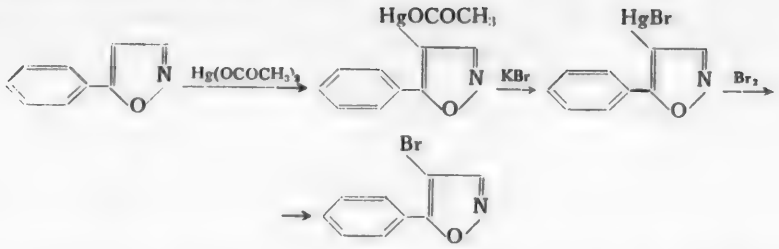
In addition to the two products indicated above, the reaction mixture contained a certain amount (15% of the total amount of reaction products) of unidentified substance, which apparently is a mixture of polynitro derivatives and destruction products.

The bromination of 5-phenylisoxazole was run under the same conditions as for the bromination of benzene, i.e., using iron catalyst and with heating. Here a 70% yield of bromo-5-phenyloxazole was obtained, the oxidation of which with potassium permanganate gave benzoic acid in 74% yield, which indicates the impossibility of having a second isomer (the product of bromination in the phenyl nucleus) present in any substantial amount.



The mercuration of 5-phenylisoxazole with mercury acetate proceeds under milder conditions than does the mercuration of benzene [5] and gives 5-phenylisoxazole mercuriacetate in 90% yield, in which connection only the isoxazole nucleus is mercurated. The 5-phenylisoxazole mercuriacetate was converted to the corresponding bromide, the bromination of which gave a product identical with the compound obtained by the direct bromination of 5-phenylisoxazole. The yields of the mercuribromide derivative and bromo-5-phenylisoxazole are quite great (respectively 98 and 68%), and consequently it is difficult to assume that any substantial amounts of

phenyl-mercurated products are formed here.



As a result, if in nitration the degree of substitution in the phenyl and in the oxazole ring is approximately the same, then in bromination and mercuration the substitution is exclusively in the isoxazole ring. It should be mentioned that the nitration and mercuration of 5-phenylisoxazole proceed under milder conditions than is the case for the analogous reactions with benzene. Bromination, proceeding under the same conditions as for the bromination of benzene, is exclusively in the isoxazole ring. All of this suggests that of the two rings found in 5-phenyloxazole, it is the isoxazole ring that is the more active.

The position of the substituents in the isoxazole ring of the 5-phenylisoxazole derivatives obtained by us is being worked upon at the present time, and as indicated above, there is basis to assume that the substituents are found in the 4-position.

EXPERIMENTAL

Nitration. Nine grams of 5-phenylisoxazole was added with vigorous stirring and cooling at −10 to −5° to 30 ml of sulfuric acid (d 1.83). To the obtained mass with cooling from −5 to −2° was added a mixture of 14 ml of nitric acid (d 1.54) and 20 ml of sulfuric acid (d 1.83), after which the reaction mixture was stirred at 15-18° for 1 hour and then poured on ice. The obtained white crystals were filtered, washed with water, and dried in a vacuum-desiccator over phosphorus pentoxide. We obtained 8.85 g of substance (75% yield) with m.p. 95-120°. Recrystallization from methyl alcohol gave 4 g (45%) of colorless crystals with m.p. 163-165°. After 2 recrystallizations from methyl alcohol the compound was obtained as colorless needle crystals with m.p. 171-172°.

Found %: N 14.75, 14.86. $C_9H_6O_3N_2$. Calculated %: N 14.73.

The mixed melting point with the substance obtained from p-nitrophenyl β-chlorovinyl ketone, was not depressed.

5-(p-Nitrophenyl)isoxazole (m.p. 171-172°) was heated for 10 hours with a water solution of potassium permanganate. p-Nitrobenzoic acid with m.p. 233° was obtained; after recrystallization from water, m.p. 237-237.5° (238° [6]). The mixed melting point with authentic p-nitrobenzoic acid was not depressed.

The mother liquor from the recrystallization of the product with m.p. 95-120° was evaporated in vacuo, the obtained crystals were filtered, and 2.7 g of substance (30% of the total amount of reaction products) with m.p. 107-109° was isolated. Evaporation of the filtrate gave 1.5 g of yellow oil, which partially crystallized on long standing. After 3 recrystallizations from methyl alcohol the compound was obtained as white crystals with m.p. 115.5-116.5°.

Found %: C 56.93, 57.16; H 3.10, 3.12. $C_9H_6O_3N_2$. Calculated %: C 56.84; H 3.15.

Nitro-5-phenylisoxazole (m.p. 115.5-116.5°) was heated for 8 hours with a water solution of potassium permanganate, and benzoic acid with m.p. 125-126° was isolated; after precipitation from the salt and recrystallization from water the compound was obtained as lustrous white crystals with m.p. 122° (122° [7]). The mixed melting point with authentic benzoic acid was not depressed.

Bromination. To a suspension of 0.1 g of iron powder in 10 g of 5-phenylisoxazole was added 11 g of bromine in drops; slight warming up of the mixture was observed. The mixture was heated on the boiling water bath until the evolution of hydrogen bromide ceased, and then it was dissolved in ether. The ether solution was washed with aqueous sodium thiosulfate solution, then with water, and the ether was evaporated in the cold; the crystals were dried over phosphorus pentoxide; yield 10.5-10.8 g (68-70%). Two recrystallizations from petroleum ether gave

the compound as colorless plates with m.p. 31-32°.

Found %: C 48.37, 48.17; H 2.61, 2.68. C_9H_6ONBr. Calculated %: C 48.24; H 2.69.

Bromo-5-phenylisoxazole is readily soluble in the common organic solvents, and is volatile with steam. B.p. 101-102° (1 mm). 0.25 g of the 5-phenylisoxazole (m.p. 31-32°) was heated for 12 hours with a water solution of potassium permanganate. We obtained 0.1 g (74%) of benzoic acid with m.p. 121-122°. The mixed melting point with authentic benzoic acid was not depressed.

Mercuration. A mixture of 13.4 g of 5-phenylisoxazole and 28.2 g of mercury acetate was heated on the water bath until all of the mercury acetate had dissolved (30 minutes). On further heating the reaction mass crystallized completely. The obtained crystalline mass was pressed on porous plate and dried. We obtained 33.9 g (90%) of 5-phenylisoxazole mercuriacetate with m.p. 163-165°. Recrystallization from dilute dioxan gave colorless needle crystals with m.p. 169-170°.

Found %: C 32.74, 32.87; H 2.30, 2.46. $C_{11}H_9O_3NHg$. Calculated %: C 32.71; H 2.24.

5-Phenylisoxazole mercuriacetate is readily soluble in dioxan and glacial acetic acid, and difficultly soluble in dichloroethane.

A solution of 36.5 g of 5-phenylisoxazole mercuriacetate in dioxan was treated with a solution of 10.75 g of potassium bromide in dioxan. The obtained precipitate was filtered and dried in vacuo over phosphorus pentoxide. We obtained 37.7 g (98%) of 5-phenylisoxazole mercuribromide with m.p. 230°, which was dissolved in 2 liters of dry dichloroethane. The obtained solution was treated with a solution of 14.2 g of bromine in 50 ml of dichloroethane, and the mixture boiled for 6 hours (until it became colorless). The dichloroethane was distilled off to dryness, and the bromo-5-phenylisoxazole was extracted from the residue with petroleum ether. Evaporation of the ether in vacuo gave 13 g (65%) of a yellow oil as residue, which crystallized completely on cooling. Vacuum-distillation gave an oil (b.p. 101-102° at 1 mm), which crystallized completely to colorless plates with m.p. 31-32°.

Found %: C 48.25, 48.28; H 2.75, 2.75. C_9H_6ONBr. Calculated %: C 48.24; H 2.69.

The mixed melting point with the bromo-5-phenylisoxazole, obtained by the direct bromination of 5-phenylisoxazole, was not depressed.

SUMMARY

1. The bromination or mercuration of 5-phenylisoxazole results in substitution only in the isoxazole ring. On nitration the substitution goes to the same degree in both the phenyl and isoxazole rings.

2. In substitution reactions of 5-phenylisoxazole the isoxazole ring is more active than the phenyl ring.

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REACTION OF AROMATIC COMPOUNDS WITH ALCOHOLS IN THE PRESENCE OF ACID CATALYSTS

III. REACTION OF PHENOL WITH DIOLS IN THE PRESENCE OF PHOSPHORIC ACID

I. P. Losev and O. V. Smirnova

Continuing our investigations of the reaction of aromatic compounds with alcohols in the presence of acidic catalysts, we selected as one of our next problems a study of the reaction of phenol with diols. As study subjects we took the 1,4- and 1,3-butanediols.

Nothing could be found in the literature on the condensation of phenols with diatomic alcohols. The condensation was run by us under conditions similar to those used for the condensation of phenols with monoatomic alcohols in the presence of acidic catalysts.

The literature on the alkylation of phenols with alcohols and ethylenic hydrocarbons is quite extensive [1-17], indicating that various products of acidic character ($AlCl_3$, H_2SO_4, solution of concd. H_2SO_4 in acetic acid, BF_3, H_3PO_4, etc.) can be used as catalysts for the reaction. In most cases the alkylation goes with the formation of para-substituted phenols. For all practical purposes the ortho-substituted derivatives are not obtained, and only in isolated cases are they described as being the main reaction products.

We ran the condensation of phenol with diatomic alcohols, and specifically with diethylene glycol, 1,3-butanediol and 1,4-butanediol, in the presence of aluminum chloride and phosphoric acid. Positive results were obtained when phenol was condensed with 1,4-butanediol in the presence of phosphoric acid. Here we obtained two compounds — 4-(p-hydroxyphenyl)butanol (I) and 1,4-bis(p-hydroxyphenyl)butane (II).

$$p\text{-}HOC_6H_4CH_2CH_2CH_2CH_2OH$$
(I)

$$p\text{-}HOC_6H_4CH_2CH_2CH_2CH_2C_6H_4OH\text{-}p$$
(II)

EXPERIMENTAL

The condensation of phenol with diethylene glycol and with 1,3-butanediol in the presence of aluminum chloride and phosphoric acid leads to the formation of tarry products, soluble in benzene, alcohols, and other organic solvents. We were unable to isolate any individual organic compounds.

The condensation of phenol (40.0 g) and 1,4-butanediol (30.0 g) in the presence of phosphoric acid (166.6 g) with heating for 10 hours at 180-200° gave a mixture of products, which separated into two layers. The upper oily layer was separated from the lower acidic layer, washed until neutral, dried over calcium chloride, and vacuum-distilled at 2 mm. Six fractions were obtained from the distillation. The first two fractions represented products that were rich in the starting phenol.

Fraction 3 after redistillation gave a substance with b.p. 212-215°, corresponding to the monophenyl ether of 1,4-butanediol with d^{20}_4 1.0334, $n^{20}D$ 1.5350, MR_D 85.77; calc. 85.84.

Fraction 4 after redistillation proved to be 4-(p-hydroxyphenyl)-butanol (I):

B. p. 232-235°, d^{20}_4 1.0352, $n^{20}D$ 1.5301, MR_D 84.5; calc. 85.0.

Found %: C 72.71, 72.83; H 8.08, 8.32. M 167.5. $C_{10}H_{14}O_2$. Calculated %: C 72.30; H 8.41. M 166.0.

The obtained product (I) was acetylated with acetic anhydride under heating. To establish the structure of (I) we oxidized it (1.5 g, dissolved in 40.0 ml CH_3COOH) with a mixture composed of 43.0 g $K_2Cr_2O_7$, 2.3 g of glacial acetic acid and 4.3 ml of water for 1 hour at 60-70°. On conclusion of reaction the following fraction was isolated:

B. p. 221-223°, d^{20}_4 1.0482, $n^{20}D$ 1.5389.

Found %: C 73.80, 73.88; H 7.14, 7.21. M 160.0. $C_{10}H_{12}O_2$. Calculated %: C 73.20; H 7.29. M 164.0.

The analysis data indicate that the product obtained in the oxidation of (I) is the hydroxyphenylbutyraldehyde. The presence of the aldehyde group was shown by qualitative tests.

Fraction 5 after redistillation gave a substance with b.p. 247-249°, which corresponds to 1,4-bis(p-hydroxyphenyl)butane (II).

Found %: C 78.84, 79.11; H 7.41, 7.34. M 238. $C_{16}H_{18}O_2$. Calculated %: C 79.34; H 7.44. M 242.

SUMMARY

1. The reaction of diethylene glycol and 1,3-butanediol with phenol in the presence of $AlCl_3$ and H_3PO_4 leads to the formation of tarry products, soluble in most organic solvents.

2. The reaction of 1,4-butanediol with phenol in the presence of H_3PO_4 leads to the formation of 4-(p-hydroxyphenyl)butanol (I) and 1,4-bis(p-hydroxyphenyl)butane (II). The optimum conditions for running this reaction is to heat the reaction mixture at 200-220° in dilute phosphoric acid (d 1.5) medium, i.e., conditions that are more drastic than those indicated by various authors in the literature for running the condensation of phenol with monoatomic alcohols. Simultaneously with (I) and (II), tarry products are also obtained in this reaction, soluble in acetone and benzene [4, 8, 15].

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CHEMISTRY OF NAPHTHACENE

VII. NITRATION OF NAPHTHACENE*

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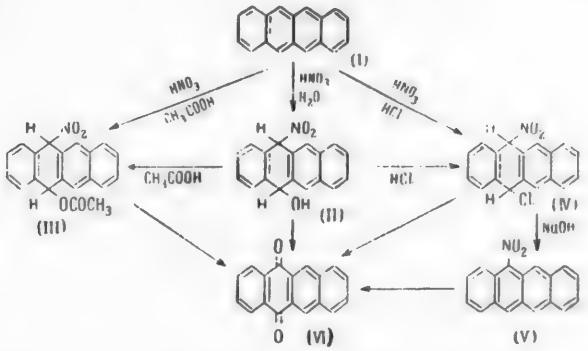
Due to the difficult availability of the hydrocarbon naphthacene, the chemistry of this compound has received comparatively little study up to now. Thus, for example, the nitration of naphthacene has not been reported in the literature. Our study of the reaction revealed that naphthacene on nitration behaves in the same manner as anthracene. Naphthacene gives unstable dihydronitro products due to the addition of nitric acid at the para-positions of one of the middle rings. Beginning at the second middle ring, addition does not proceed, apparently for the reason that addition at the first ring separates the molecule into two isolated aromatic systems – a benzene and a naphthalene system, neither having an active meso-position.

The nitration products of naphthacene, obtained in the present study, and their mutual transformations, are depicted in the scheme.



The first intermediate product in the nitration of naphthacene is 9-nitro-10-hydroxydihydronaphthacene (II). It is easily formed by treating naphthacene under cooling to 0-3° with nitric acid (d 1.36) or by reacting nitric acid at the same temperature with a suspension of naphthacene in glacial acetic acid. In the last case, as soon as a clear solution is obtained, it is poured into water, and here 9-nitro-10-hydroxydihydronaphthacene is obtained as a precipitate. If the reaction mass is not poured into water, but instead the stirring is continued, then the 9-nitro-10-hydroxydihydronaphthacene is easily acetylated, and soon yellow needles of 9-nitro-10-acetoxydihydronaphthacene (III) deposit from solution. The corresponding anthracene derivative is also known [1].

9-Nitro-10-chlorodihydronaphthacene (IV) was obtained in the same manner as the corresponding anthracene derivative [2] by treating a suspension of naphthacene in glacial acetic acid with nitric acid (d 1.36) at 0-3°, followed by the addition of concd. HCl to the obtained clear solution of 9-nitro-10-hydroxydihydronaphthacene. The chloro compound can also be obtained from 9-nitro-10-hydroxydihydronaphthacene if the latter is dissolved in glacial acetic acid and then treated with concd. HCl solution with cooling.

* Communication VI: J. Gen. Chem. 20, 1711 (1950). (Original Russian pagination. See C. B. Translation.)

The obtained dihydronitro derivatives of naphthacene, the same as the corresponding products of the anthracene series, are quite unstable compounds. When heated in organic solvents, in an attempt to recrystallize them, they are easily and completely converted to pure p-naphthacenequinone. Here neither anaquinone nor other products could be found. This indicates that during nitration only addition at the para-positions took place.

Judging from the constants and the analysis data, the obtained dihydronitro derivatives represent quite pure compounds without further purification. The most stable 9-nitro-10-acetoxydihydronaphthacene can be recrystallized from glacial acetic acid heated to 50°.

The treatment of 9-nitro-10-chlorodihydronaphthacene with dilute alkali in the cold yields a red water-soluble substance, in all probability being the sodium salt of the acid form of the dihydronitro compound.* Probably, it is also possible to obtain other dihydronitro products in the naphthacene series, similar to those described for anthracene [4], for example, 9-nitro-10-methoxy-(ethoxy)-dihydro derivatives, etc.

We were able to obtain the most interesting nitro product of the naphthacene series, namely 9-nitronaphthacene (V), only from 9-nitro-10-chlorodihydronaphthacene (IV) by treating the latter with 30% sodium hydroxide solution at 50° for several hours. When the other dihydronitro compounds (II) and (III) were treated with either alkali solution, pyridine or alcoholic caustic solution, with slight heating, we were unable to obtain the nitronaphthacene, and instead p-naphthacenequinone (VI) was obtained in all cases. It is possible that under certain conditions these transformations take place, as is the case in the anthracene series [5].

The preparation and study of 9-nitronaphthacene was complicated by its extreme instability. It is much less stable than 9-nitroanthracene, and when heated in various organic solvents, or when the solutions are allowed to stand in the cold, especially in the light, it suffers rapid decomposition and is converted to p-naphthacenequinone. 9-Nitronaphthacene can be recrystallized if it is added to boiling glacial acetic acid, and after filtering, the solution is cooled rapidly. In the dry crystalline state it is stable and can be stored. In contrast to the yellow 9--nitroanthracene, 9-nitronaphthacene has a red color.

The color of the obtained products with concd. H_2SO_4 and their fluoroescence under an ultraviolet lamp can serve as a rapid qualitative test for their identification. All of the derivatives containing a nitro group give a deep blue coloration with concd. H_2SO_4, in contrast to a green color for naphthacene, and a red color for p--naphthacenequinone. 9-Nitronaphthacene does not fluoresce under an ultraviolet lamp, in contrast to all of the other compounds described here, which give either a yellow or orange luminescence.

EXPERIMENTAL

Naphthacene was obtained by the method described in [5] from ethyne diphthalide by distillation with zinc dust.

9-Nitro-10-hydroxydihydronaphthacene (II). To a suspension of 0.2 g of finely divided napthacene in 4 ml of glacial acetic acid was gradually added with good stirring 4 ml of HNO_3 (d 1.36), previously freed of nitrogen oxides by blowing with air. This temperature of the reaction mass was kept constant at 0-3°. After stirring for 20-25 minutes the suspension was converted to a clear solution, which was poured into cold water. The resulting light-yellow microcrystalline precipitate was filtered, repeatedly washed with water, and dried in a vacuum-desiccator over $CaCl_2$. Yield 0.21 g (quantitative). M.p. 90-95°.

Found %: N 4.92. Active H 1.2. $C_{18}H_{12}O_3N$. Calculated %: N 4.79. Active H 1.0.

The compound is readily soluble in alcohol, benzene, acetic acid and dioxan but when recrystallized from a hot solvent it is quantitatively converted to p-naphthacenequinone, obtained as long slender yellow needles with m.p. 285-290°. If the compound is dissolved in dioxan at room temperature, followed by evaporation of the solvent in vacuo, then it becomes possible to obtain 9-nitro-10-hydroxydihydronaphthacene as coarse transparent prisms. M. p. 90-95°.

9-Nitro-10-hydroxydihydronaphthacene can also be obtained if naphthacene is nitrated in the absence of a solvent: 0.2 g of powdered naphthacene was stirred at 0-5° for several hours with 20-25 ml of HNO_3 (d 1.36). The suspension gradually changed from an orange to a light-yellow color. The microcrystalline precipitate was filtered, washed with water, and dried in vacuo at room temperature. M.p. 90-95°, and not depressing the melt-

* A similar salt was described in the anthracene series [3].

ing point when mixed with the compound described above.

9-Nitro-10-acetoxydihydronaphthacene (III). This compound was obtained under conditions similar to the preceding experiment, but here the obtained clear reaction mass was not poured into water, but instead it was allowed to stand at 0-5°. The yellow needles or prisms that deposited in approximately an hour were filtered, washed with water, and air-dried. Yield 0.22 g (quantitative). M.p. 270-275°. Considerably less soluble in the cold in acetic acid, alcohol, and other solvents, than the hydroxy derivative (II). When recrystallized from hot solvents it also suffers quantitative conversion to p-naphthacenequinone. We found that the crude product could be recrystallized from acetic acid, heated to 50-60°.

Found (for the unrecrystallized product) %: N 4.55. $C_{20}H_{15}O_4N$. Calculated %: N 4.20.

9-Nitro-10-acetoxydihydronaphthacene can also be obtained from the hydroxy compound (II). 9-Nitro-10--hydroxydihydronaphthacene (0.1 g) was dissolved with cooling in 4-5 ml of glacial acetic acid. The solution on standing soon began to deposit crystals of the acetyl derivative (III). M.p. 270-275°, not depressing the melting point when mixed with the compound obtained above.

9-Nitro-10-chlorodihydronaphthacene (IV). Pulverized naphthacene (0.2 g) was suspended in 4 ml of glacial acetic acid and 4 ml of HNO_3 (d 1.36) was added with cooling to 0-3°. As soon as the suspension had changed to a clear solution a mixture of 4 ml of hydrochloric acid (d 1.19) and 2 ml of glacial acetic acid was added, and the reaction mass was stirred for 1 hour at a temperature not exceeding 5°. The yellow finely crystalline precipitate (needles) was filtered, washed with 2-3 ml of acetic acid, and then well with water. Yield 0.21 g. M.p. 130-135° (with decompn.).

Found %: N 4.69, 4.60. $C_{18}H_{12}O_2NCl$. Calculated %: N 4.51.

The chlorine content was 1-2% less than the calculated (9-10% instead of 11.48%). Evidently the product contains the hydroxy and acetoxy compounds (II and III) as impurities. It proved that we could not recrystallize the compound, since when heated in solvents it is quantitatively converted to p-naphthacenequinone, while if it is dissolved in benzene, dioxan or chloroform in the cold, followed by evaporation of the solvent, a viscous mass is obtained.

9-Nitro-10-chlorodihydronaphthacene can also be obtained from the hydroxy product (II) if the latter is dissolved in glacial acetic acid, and the solution treated with concentrated hydrochloric acid at 3-5°.

9-Nitronaphthacene (V). The moist freshly prepared 9-nitro-10-chlorodihydronaphthacene (IV), obtained from 0.2 g of naphthacene, was rubbed in a small dish with 4 ml of 30% NaOH, with heating to 50° on the water bath. The slurry of crystals gradually assumed a red color. After 2 hours the reaction mass was diluted with water and the precipitate filtered, washed well with water, and dried in a vacuum-desiccator. Yield 0.17-0.18 g. Red microcrystalline powder, m.p. 190-192° (with decompn.).

Found %: N 5.00. $C_{18}H_{11}O_2N$. Calculated %: N 5.12.

9-Nitronaphthacene can be recrystallized from acetic acid. For this the moist freshly obtained 9-nitronaphthacene is dissolved in glacial acetic acid (5-6 ml per 0.2 g), previously heated to the boil, and the hot solution is rapidly filtered and cooled; clusters of brick-red needles deposit. M.p. 190-192°. But if the acetic acid solution is boiled for only a few minutes, then the pure p-naphthacenequinone is obtained as long yellow needles, m.p. 285-290°.

SUMMARY

1. It was established that the nitration of naphthacene gives the addition product — 9-nitro-10-hydroxydihydronaphthacene (II), which when reacted with acetic acid is converted to 9-nitro-10-acetoxydihydronaphthacene (III), and when reacted with concentrated hydrochloric acid is transformed to 9-nitro-10-chlorodihydronaphthacene (IV).

2. 9-Nitronaphthacene (V) was obtained by the action of 30% NaOH on 9-nitro-10-chlorodihydronaphthacene (IV).

3. It was established that the dihydronitro derivatives of naphthacene (II-IV) and 9-nitronaphthacene are even less stable than the corresponding compounds of the anthracene series, and are easily converted when heated

in solvents or without a solvent to p-naphthacenequinone.

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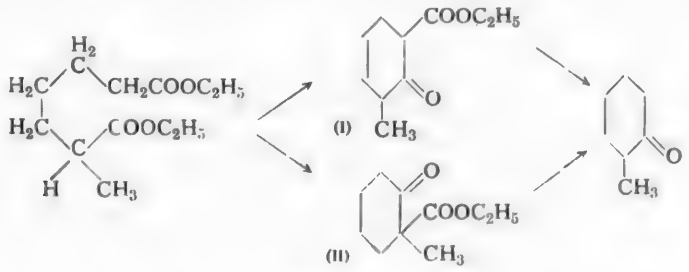
INVESTIGATION IN THE FIELD OF THE DIECKMANN REACTION

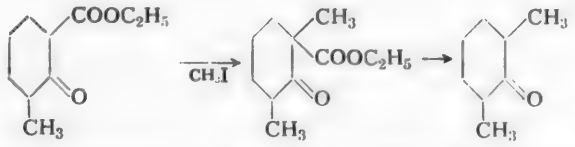
III. CYCLIZATION OF THE DIETHYL ESTER OF α-METHYLPIMELIC ACID

N. S. Vul'fson and V. I. Zaretskii

Dieckmann [1] described the cyclization of the diethyl ester of α-methylpimelic acid and considered that this reaction gave 2-methyl-6-carbethoxycyclohexanone, which, however, was not isolated in a pure form. The author proposed a structure for the product obtained on the basis of a qualitative reaction with ferric chloride, the preparation of a copper salt and the conversion to 2-methylcyclohexanone by hydrolysis and decarboxylation. However, as the scheme shows, the formation of 2-methylcyclohexanone from the diethyl ester of α-methylpimelic acid may proceed by two paths and, consequently, the formation of 2-methylcyclohexanone cannot be considered as proof of the structure of the cyclic β-ketoester formed as an intermediate.



In continuing the study of the mechanism of cyclization of esters of unsymmetrical dicarboxylic acids by Dieckmann's method [2], we set out to establish more accurately the structure of the cyclic β-ketoester, formed during the cyclization of the diethyl ester of the α-methylpimelic acid. The only cyclization product was β-ketoester (I). We could not detect the formation of β-ketoester (II). With an aqueous ferric chloride solution the cyclization product gave a violet-red color and had constants different from those of 2-methyl-2-carbethoxycyclohexanone, which we obtained during the synthesis of the diethyl ester of α-methylpimelic acid. The structure of the cyclization product was confirmed by its methylation and subsequent decarboxylation of the 2,6-dimethyl-6-carbethoxycyclohexanone obtained to 2,6-dimethylcyclohexanone, described previously by Ruzicka [3].



2-Methyl-2-carbethoxycyclohexanone (II) should not be methylated under similar conditions and this was confirmed experimentally. The unusual formation of the β-ketoester (I) in the cyclization of the diethyl ester α-methylpimelic acid is, apparently, explained by the increase in electron density at the α-carbon atom due to the I-effect of the CH_3 group, which hinders proton dissociation and the formation of the organic anion, necessary for cyclization.

EXPERIMENTAL

2-Carbethoxycyclohexanone was prepared by the method of Schneider, Brooks and Shapiro [4]; after redistillation the material had b.p. 77-83° at 2 mm, $n^{20}D$ 1.4810.

2-Methyl-2-carbethoxycyclohexanone was prepared by a slightly modified method [5].

To a mixture of 103.5 g of 2-carbethoxycyclohexanone and 50 ml of methyl iodide, cooled to −15°, a solution of sodium methylate (from 15.1 g of sodium and 183 ml of methanol) was added over a period of 15 minutes at −13° to −10°. The mass gradually thickened but when the temperature was raised to 0°, it became liquid again. The mass was stirred for 3 hours at −5° and left overnight at −5° (in a refrigerator). The excess methyl iodide (~19.5 g) and part of the methanol was distilled off on a boiling water bath; the total volume of the distillate was 70 ml. The cooled residue was treated with 700 ml of water, shaken in a separating funnel and extracted with ether (5 × 150 ml). The ether solution was washed with 15% potassium hydroxide solution in 75-ml portions until it gave a negative reaction with an aqueous solution of ferric chloride, washed with water until the wash water gave a neutral reaction with brilliant yellow paper and then dried over anhydrous sodium sulfate. The solvent was distilled off and the residue distilled in vacuum. The yield of 2-methyl-2-carbethoxycyclohexanone was 96.4 g (86%) and the product had b.p. 80-81° at 2.5 mm, $n^{20}D$ 1.4540, d^{20}_4 1.044. It did not give a color reaction with ferric chloride solution. According to literature data the b.p. is 113-114° at 10-11 mm [5], 100-104° at 9 mm [6].

Diethyl ester of α-methylpimelic acid [7]. To a solution of sodium ethylate (from 2.2 g of sodium and 100 ml of anhydrous alcohol) was added 92 g of 2-methyl-2-carbethoxycyclohexanone, the mixture boiled for 6 hours and then cooled, 400 ml of water added, the mixture acidified to pH ~ 6.5 with acetic acid and the product extracted with ether (200 + 100 ml) and dried over anhydrous sodium sulfate. The solvent was distilled off and the residue distilled in vacuum to give a fraction boiling at 110.5-118° at 3.5 mm, which was redistilled to give 81 g (70%) of the ester with b.p. 115-118° at 4 mm, $n^{20}D$ 1.4318, d^{20}_4 0.9823. According to the literature data it has b.p. 140° at 12 mm [8].

Cyclization of the diethyl ester of α-methylpimelic acid. 34.5 g of the diethyl ester of α-methylpimelic acid and 0.3 ml of anhydrous alcohol was quickly added to a suspension of 5 g of powdered sodium in 125 ml of benzene (dried over sodium). The evolution of bubbles of hydrogen began immediately and the mass warmed up very slowly. It was carefully heated to boiling and stirred until the sodium completely disappeared (~ 3 hours). The temperature of the vigorously boiling mass fell from 81.5 to 77.5° over 30-40 minutes. The mass was cooled to −7°, when a voluminous precipitate formed and the temperature rose to 3°. The thick suspension was poured onto 100 g of ice (in a cooling mixture) and acidified to congo with dilute (1 : 1) hydrochloric acid, the benzene layer separated, the aqueous layer extracted with 50 ml of benzene and the combined benzene solution washed successively with 5% soda solution (40 ml) and water (50-ml portions) until neutral to brilliant yellow paper. The washed solution was dried with anhydrous sodium sulfate, the solvent distilled off and the residue distilled in vacuum to give 2-methyl-6-carbethoxycyclohexanone (I); the yield was 19.4 g (70%), the b.p. 84.5-86° at 2.5 mm, $n^{20}D$ 1.4720, d^{20}_4 1.0455; with an aqueous solution of ferric chloride the product immediately gave a violet red color; MR_D 49.32; calculated for the enol 48.89, for the ketone 47.85. According to literature data: b.p. 97° at 4 mm [9].

Found %: C 64.81; H 8.87. $C_{10}H_{16}O_3$. Calculated %: C 65.22; H 8.69.

2,6-Dimethyl-6-carbethoxycyclohexanone. Over a period of 10 minutes, a solution of sodium methylate (from 1.35 g of sodium and 16 ml of dry methanol) was added dropwise to a stirred mixture of 10 g of 2-methyl-6-carbethoxycyclohexanone and 4.6 g of methyl iodide at −10° to −7°. Five minutes after the end of the addition, the mass thickened at −6° and it was kept at a temperature of from 0 to −3° for 4 hours and then overnight at 4-5°. The solvent was distilled off in vacuum (58-60 mm) with a bath temperature of 50°, 100 ml of water added to the cooled residue, which was extracted with ether (4 × 25 ml), and the ether solution washed several times with 20-ml portions of 15% potassium hydroxide solution until it gave a negative qualitative reaction with an aqueous solution of ferric chloride and then with water (25-ml portions) until neutral to brilliant yellow paper. The solution was dried with anhydrous sodium sulfate, the solvent distilled off and the residue vacuum distilled to give 2,6-dimethyl-6-carbethoxycyclohexanone; the yield was 8.2 g (76.8%), the b.p. 79-85° at 2.5 mm, $n^{20}D$ 1.4528; the product did not give a color with ferric chloride. According to the literature data: b.p. 112-118° at 12 mm [6].

Found %: C 66.84; H 9.05. $C_{11}H_{18}O_3$. Calculated %: C 66.66; H 9.09.

2,6-Dimethylcyclohexanone [3]. 7.7 g of potassium hydroxide was dissolved with boiling in 11.5 ml of anhydrous methanol, the hot solution quickly cooled to −8°, 9 g of 2,6-dimethyl-6-carbethoxycyclohexanone added in one portion to the thick mass, which was externally cooled in a mixture of ice and salt, and the mixture shaken and left at room temperature for 9 days. Part of the solvent was distilled off in vacuum (~ 60 mm) with a bath temperature of ~25°, 50 ml of water added to the residue, the mass shaken, the oil which separated dissolved in 50 ml of ether and the aqueous layer extracted with ether (2 × 50 ml). The aqueous layer was acidified with concentrated hydrochloric acid until strongly acid to congo and boiled for 10 hours, the very small amount of oil which separated extracted with ether and the extract added to the main ether solution. The combined ether solution was washed with water and dried over anhydrous sodium sulfate. The solvent was distilled off and the residue vacuum distilled to give 2,6-dimethylcyclohexanone; the yield was 2.5 g (44%), the b.p. 61-61.5° at 12-13 mm, $n^{20}D$ 1.4465. According to literature data, b.p. 62° at 12 mm, $n^{20}D$ 1.4481 [5].

Found %: C 76.44; H 11.20. $C_8H_{14}O$. Calculated %: C 76.19; H 11.11.

The semicarbazone had m.p. 176-177°; according to literature data: m.p. 176° [3].

Found %: C 59.01; H 9.33. $C_9H_{17}ON_3$. Calculated %: C 59.03; H 9.29.

Attempted methylation of 2-methyl-2-carbethoxycyclohexanone. 28 g of 2-methyl-2-carbethoxycyclohexanone was treated with methyl iodide as in the case of 2-methyl-6-carbethoxycyclohexanone and we obtained 19.2 g of material with b.p. 78.5-85° at 2 mm, $n^{20}D$ 1.4555-1.4570.

2-Methylcyclohexanone. 8.4 g of the methylation product obtained above was boiled for 20 hours with 100 g of ~20% sulfuric acid. The reaction mixture was extracted with ether (3 × 50 ml) and the ether solution washed with water, dried and distilled. We obtained 2-methylcyclohexanone with b.p. 160-164° at 740 mm, $n^{20}D$ 1.4480, d^{20}_4 0.9217. According to literature data: b.p. 166°, $n^{20}D$ 1.4483 [10]; $n^{20}D$ 1.4475 [11], d^{20}_4 0.9231 [12]. The semicarbazone had m.p. 191-192° (from alcohol). It did not depress the melting point of 2-methylcyclohexanone semicarbazone. According to literature data 2-methylcyclohexanone semicarbazone has m.p. 191° [10, 13].

SUMMARY

Cyclization of the diethyl ester of α-methylpimelic acid by Dieckmann's method was studied. It was shown that 2-methyl-6-carbethoxycyclohexanone was the primary reaction product; the formation of 2-methyl-2-carbethoxycyclohexanone was not observed. The structure of 2-methyl-6-carbethoxycyclohexanone was confirmed by preparing 2,6-dimethylcyclohexanone by methylation with methyl iodide, followed by hydrolysis and decarboxylation.

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CATALYTIC CONVERSIONS OF HALOGEN DERIVATIVES OF THE AROMATIC SERIES

IV. A STUDY OF THE MECHANISM OF THE CATALYTIC ISOMERIZATION OF MONOCHLORONAPHTHALENES USING LABELED ATOMS

N. N. Vorozhtsov, jr. and V. A. Koptiug

In studying monobromonaphthalene isomerization in the presence of ferric chloride, Dutch investigators [1] assumed that this reaction was due to the reversibility of the bromination process both in liquid phase and vapor phase isomerization.

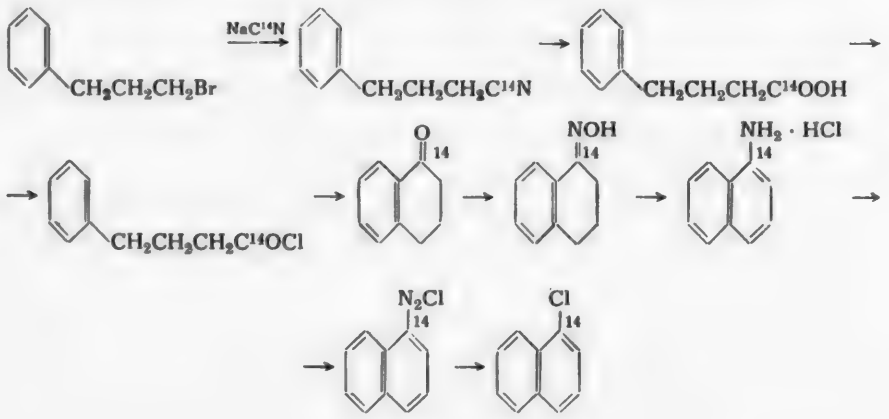
$$\alpha\text{-}C_{10}H_7Br + HBr \rightleftarrows C_{10}H_8 + Br_2 \rightleftarrows \beta\text{-}C_{10}H_7Br + HBr$$

Under these conditions isomerization was actually accompanied by the formation of naphthalene and dibromonaphthalenes.

However, in work devoted to the study of vapor phase catalytic isomerization of monochloro- and monobromonaphthalenes over aluminum oxide and aluminosilicate, one of us et al. [2, 3] obtained data which seemed to indicate an intermolecular course for the reaction.*

This work shows that in the isomerization of 1-chloronaphthalene-1-C^{14} on an aluminosilicate catalyst at 355-365°, mainly 2-chloronaphthalene-1-C^{14} is formed. This result excluded the possibility of the intermediate formation of naphthalene, as in this case isomerization of 1-chloronaphthalene-1-C^{14} would give an equimolecular mixture of 2-chloronaphthalenes, labeled in positions 1, 4, 5 and 8.

The 1-chloronaphthalene-1-C^{14}, which has not been described previously, was synthesized by the scheme



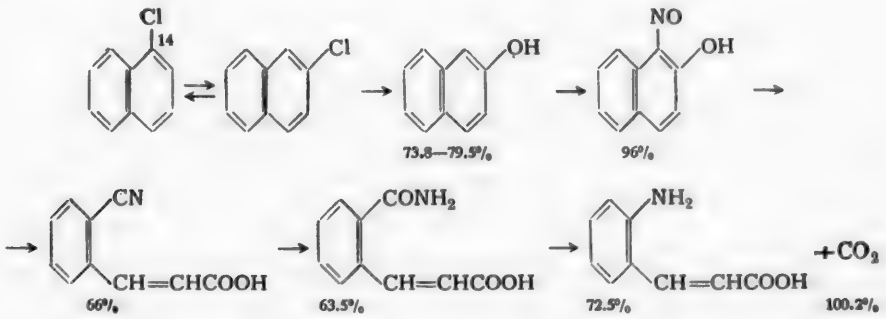
* Analogous data were previously obtained in the field of liquid phase isomerization by Brezhneva and Roginskii [30] who used radioactive bromine to show that in the isomerization of monobromonaphthalenes in carbon disulfide in the presence of aluminum bromide, the bromine exchange in monobromonaphthalene proceeded much more slowly than the isomerization.

γ-Phenylpropyl bromide and sodium cyanide gave γ-phenylbutyric acid, labeled with radiocarbon in the carboxyl group, and this was converted by Johnson and Glenn's method [4] to 1-keto-1,2,3,4-tetrahydronaphthalene-1-C^{14} (α-tetralone-1-C^{14}), which was isolated as the oxime in 92.8% yield (calculated on the initial cyanide).

To convert the 1-keto-1,2,3,4-tetrahydronaphthalene-1-C^{14} oxime to 1-naphthylamine-1-C^{14} we used the reaction described by Schroeter [5], which proceeds on heating the oxime with acetic anhydride in glacial acetic acid in a current of hydrogen chloride. This reaction, carried out by a method we developed,* gave a 51.8% yield of 1-naphthylamine-1-C^{14} hydrochloride. A mixture of α- and β-naphthols (16.8% yield) was isolated as a side product.

1-Chloronaphthalene-1-C^{14} was prepared in ~50% yield from 1-naphthylamine-1-C^{14} hydrochloride by Sandmeyer's reaction [6, 7].

1-Chloronaphthalene-1-C^{14} was isomerized on an aluminosilicate catalyst in a current of hydrogen chloride at 355-365°. The 2-chloronaphthalene thus formed was degraded to split out the carbon atom in position 1, by the scheme



2-Chloronaphthalene was treated with 0.8 N sodium hydroxide solution at 365° to give 2-naphthol and nitrosation of the latter [8] gave 1-nitroso-2-naphthol.

The C_1-C_2 bond of the naphthalene nucleus was split by rearranging 1-nitroso-2-naphthol into cis-o-cyanocinnamic acid (Beckmann rearrangement of the 2nd type), by treatment with p-toluenesulfonyl chloride in an alkaline medium [9]. Boiling the cis-o-cyanocinnamic acid obtained with dilute hydrochloric acid gave trans-o-carbamidocinnamic acid [10], which was degraded by the Hofmann reaction (treatment with sodium hydrobromite) to give trans-o-aminocinnamic acid and carbon dioxide. The latter contained the carbon from position 1 in the 2-chloronaphthalene molecule.

The results of measuring the radioactivity of trans-o-carbamidocinnamic and trans-o-aminocinnamic acids and the carbon dioxide are given in the table.

Compound	Radioactivity	
	μC/ mole	%
o-$C_6H_4(CONH_2)CH=CHCOOH$	2006 ± 19	100
o-$C_6H_4(NH_2)CH=CHCOOH$	125 ± 0.5	6.2
CO_2	1855	92.5

Thus, 93.8% of the 2-isomer formed during 1-chloronaphthalene-1-C^{14} isomerization consisted of 2-chloronaphthalene-1-C^{14} and this indicated that at least 91.7% ** of the 1-chloronaphthalene molecules were isomerized to 2-chloronaphthalene without the intermediate formation of naphthalene.

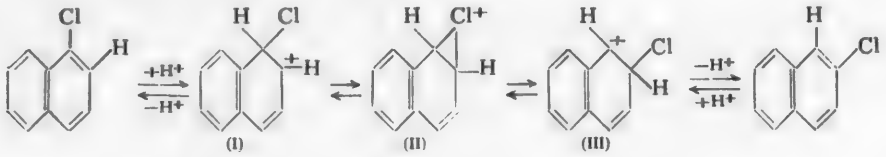
* The work on the mechanism of this reaction will be described in another paper.

** $(100 - \frac{6.2}{3} \cdot 4) = 91.7$.

The retention of 6.2% of the radioactivity by trans-o-aminocinnamic acid may be due to two reasons: partial isomerization by an intermolecular mechanism or the presence of some rearrangement during the preparation of 1-chloronaphthalene-1-C^{14}, which resulted in the formation of 1-chloronaphthalene with the radiocarbon in a different position.

The first hypothesis is supported by the fact that isomerization of monochloronaphthalenes at 550° gave 29.4% of naphthalene [3]. Therefore, it is possible that the retention of 6.2% of activity by trans-o-aminocinnamic acid is due to partial (8.3%) isomerization at 355-365° by an intermolecular mechanism. However, this cannot yet be confirmed with the available data.

The reversible transfer of the halogen during the isomerization of monohalonaphthalenes from position 1 to position 2 may be represented by the following mechanism.

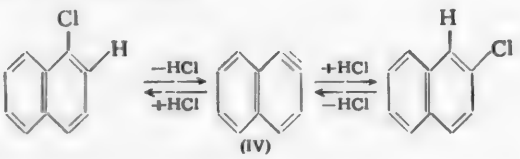


The carbonium ions (I) and (III), formed by the addition of a proton to a halonaphthalene molecule, are analogous to the intermediate cations, formed in electrophilic halogenation of naphthalene (cf. [1]). The conversion (I) ⇌(III) is readily understood if one considers the capacity of halogen atoms for donating one of their unshared electron pairs to form a second bond. The intermediate formation of halonium compounds, similar to (II), was postulated earlier for a series of reactions (see [11] for review of this problem), for example, for the addition of halogen at a double bond [12]. Recently Sandin and Hay [13] and then A. N. Nesmeianov et al. [14] were able to prepare bromonium and chloronium salts. This considerably strengthened the basis for the hypothesis on the formation of intermediate compounds of the halonium salt type.

Fluoronium compounds have not been obtained up to now. This is apparently the result of the high ionization potential of fluorine as compared with that of carbon (ionization potentials in volts: C 11.2, Br 11.8, Cl 13.0, F 18.6) and explains the absence of isomerization in the case of monofluoronaphthalenes [3].

The need for a proton for isomerization to proceed explains why halonaphthalenes isomerize especially smoothly in the presence of hydrogen halides (without them, the catalyst provides the protons).

Another possible mechanism is the following



Huisgen [15] assumed the intermediate formation of (IV) in order to explain the fact that phenyllithium treatment of both 1- and 2-fluoronaphthalene followed by carboxylation gave a mixture of 1-phenyl-2-carboxylic and 2-phenyl-1-carboxylic acids of naphthalene of the same composition. Witting [16] and Roberts [17] confirmed this assumption by proving the intermediate formation in a series of reactions of cyclohexadienyne, of which (IV) is an analog.

The intermediate formation of (IV) was also accepted as a working hypothesis [18] to explain the isomeric conversions of naphthalene derivatives and, in particular, to explain the isomerization of deuteronaphthalenes when their vapor was passed over silica gel.

It should be noted, however, that the intermediate formation of a compound of type (IV) is characteristic of reactions proceeding under conditions when there is the possibility of the formation of a carbanion as a result of the elimination of the hydrogen atom, situated in the position ortho to the halogen, as a proton [16, 17]. This occurs, for example, under the effect of such strong bases as an NR_2^- ion.

However, in our case of chloronaphthalene isomerization on an acid catalyst in the presence of hydrogen

chloride (as in the case of deuteronaphthalene isomerization on silica gel [18]) such conditions for carbanion formation do not exist, which makes the mechanism with the intermediate formation of (IV) questionable.

Such a mechanism for halonaphthalene isomerization is also contrary to the fact that isomerization of chloro- and bromonaphthalenes in the presence of hydrogen fluoride does not give fluoronaphthalenes [3].

From these considerations it appears to us that the mechanism providing for the intermediate formation of halonium salts in the isomerization of halonaphthalenes is better substantiated.

The exchange of halogen in the reaction of halonaphthalenes with hydrogen halides, observed in previous work [3], should be considered not as a result of isomerization, but as a parallel process. This was confirmed by the fact that under conditions when fluoronaphthalenes were not isomerized, fluorine was, all the same, substituted by chlorine [3].

EXPERIMENTAL

Measurement of the radioactivity of the preparations. The preparations were converted into barium carbonate using a Van Slyke "wet" combustion.

Into flask 1 of the apparatus illustrated in Fig. 1 (a modified form of the apparatus of Lindenbaum et al. [19]) was placed a sample of the substance containing 8-9 mg of carbon, in a quartz boat, and 1.1 g of a mixture of potassium iodate and potassium dichromate (2 : 1). 15 ml of ~0.2 N barium hydroxide solution, containing 20 g of barium chloride per liter, was placed in trap 2 and the system evacuated through taps 3 and 4 to a residual pressure of 20 mm. Taps 3 and 5 were closed, the stopper with tap 4 was removed and the funnel 6 charged with 10 ml of a mixture of 20% oleum (chemically pure) and 88% phosphoric acid [20], after which the funnel was closed with a tube filled with ascarite. Almost the whole of the liquid mixture was released through tap 5 into flask 1, whose contents were then heated to boiling with a small flame, boiling was continued for 10 minutes and then the mixture was left for 30 minutes. During this time the suspension of barium carbonate in trap 2 rose up the bubbler tube. This was prevented by carefully admitting air through tap 5. Then the suspension of barium carbonate was quickly transfered to a titration flask (CO_2-free water was used for rinsing) and the excess barium hydroxide titrated with 0.1 N hydrochloric acid in the presence of phenolphthalein. The carbon content of the substance was calculated from the hydrochloric acid consumed (control on completeness of combustion).

For the preparation of samples for radioactivity measurement from the barium carbonate suspension, we used the method described in [21], with the only difference that the guard ring underneath also had a flange, which covered irregularities in the edges of the sample. With a sample surface of 5.02 cm^2 (diameter 25.3 mm), the uncovered part amounted to 3.80 cm^2 (diameter 22.0 mm). The suspension of barium carbonate was kept for 12 hours at room temperature before filtration.

The activity of the sample was measured on apparatus B with an end window counter with a mica window thickness of 1.3 mg/cm^2 and a resolving time of $2.2 \cdot 10^{-4}$ sec and the separation between the sample surface and the window was 15 mm.

In all cases the samples were "infinitely" thick, i.e., thicker than 25 mg/cm^2. The counting time for the samples was chosen so that the relative mean square error of measurement was not greater than 1%.

The count rate found was corrected for background, the resolving capacity of the counter and its counting efficiency. From the corrected count rate (R_{∞}), we calculated the absolute molar activity from a slightly modified form of Vasil'ev's formula [21]

$$A = 197000 \frac{1.46\, C_E \cdot b \cdot R_{\infty}}{S} \cdot n\mu C/\text{mole},$$

where n is the number of carbon atoms in a molecule of the given compound. The coefficient C_E for our apparatus equalled $4.25 \cdot 10^{-6}$ μC·min/count.

γ-Phenylpropyl bromide. A mixture of 200 g of γ-phenylpropyl alcohol ($n^{20}D$ 1.5245), 600 g of 40% hydrobromic acid and 295 g of 96% sulfuric acid was boiled for 14 hours; the reaction product was steam distilled, washed with concentrated sulfuric acid, soda solution and water, dried with calcium chloride and distilled in vacuum. The yield of γ-phenylpropyl bromide was 259 g (88.7%) and the material had b.p. 109° (12 mm), $n^{20}D$ 1.5445.

γ-Phenylbutyric acid labeled with C^{14}. A solution of 24.0 g (120.4 mmoles) of γ-phenylpropyl bromide, 0.08 g (1.6 mmoles) of radioactive sodium cyanide (activity ~1.3 mC) and 5.20 g of 85.5%* sodium cyanide (90.6 mmoles of 100% cyanide) in 140 ml of ethyl alcohol and 20 ml of water was heated in a flask with a ground joint condenser on a glycerol bath at 100° (bath temperature) for 27.5 hours. To the solution of γ-phenylbutyronitrile obtained was added a solution of 20.6 g (367 mmoles) of potassium hydroxide in 40 ml of ethyl alcohol and 20 ml of water and the solution heated at 100° for a further 30 hours. Then 170 ml of alcohol was distilled off, 50 ml of water added and the neutral substances steam distilled off. The solution left in the flask was filtered into the flask of a continuous extractor [23], acidified with 45 ml of hydrochloric acid (d 1.172; 410 mmoles) and extracted with benzene (125 ml) for 13 hours. The γ-phenylbutyric acid was isolated from the dried benzene solution by evaporation in vacuum at a bath temperature of 50-60°

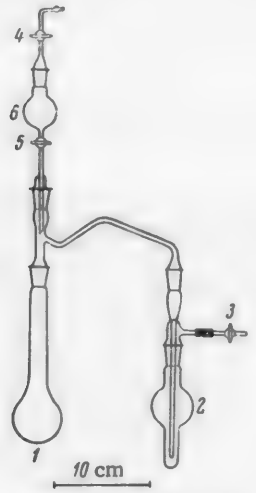


Fig. 1. Apparatus for combustion of materials (according to Van Slyke).
1) Combustion flask; 2) trap with barium hydroxide solution; 3, 4, 5) taps; 6) dropping funnel.

1-Keto-1,2,3,4-tetrahydronaphthalene-1-C^{14} and its oxime. 21.5 g (103 mmoles) of phosphorus pentachloride was added in small portions to the impure γ-phenylbutyric acid. When the evolution of hydrogen chloride ceased, the mixture was heated to 50° (bath temperature) and kept at that temperature for 5 minutes; 10 ml of anhydrous, thiophene-free benzene was added and a mixture of benzene and volatile phosphorous compounds was distilled off in vacuum at a bath temperature of 60-70°. The addition and distillation of the benzene was repeated 4 more times.

The γ-phenylbutyryl chloride obtained was dissolved in 24 ml of anhydrous benzene and after 25 minutes added to a suspension of 17.5 g (131 mmoles) of anhydrous aluminum chloride in 60 ml of anhydrous, thiophene-free benzene, which was stirredand cooled. The temperature of the reaction mixture was kept below 10°. After the addition of the acid chloride, the reaction mixture was stirred for 35 minutes at 6-10°, then in 30 minutes the temperature was raised to 22° and kept there for 3 hours and the reaction mixture left overnight.

With stirring, 100 ml of dilute hydrochloric acid (1 : 1) (the temperature of the mixture was kept below 15°) was added to the mixture obtained and the mass kept at 10° for 30 minutes. The two-layer solution was filtered off, the organic layer separated and the aqueous layer extracted three times with ether. The organic layer was washed with sodium bicarbonate solution and water, dried with potassium carbonate and the solvent distilled off in vacuum.

The α-tetralone-1-C^{14} obtained, 12.7 g (183 mmoles) of hydroxylamine hydrochloride and 12.8 g (92.5 mmoles) of potassium carbonate were dissolved with heating in 100 ml of methyl alcohol and 45 ml of water and the solution boiled for 45 minutes. Activated charcoal (~ 0.5 g) was added to the solution, which was heated for a further 10 minutes and filtered through a heated funnel. The filter was washed with 50 ml of boiling methyl alcohol. When the methanol solution was cooled, the α-tetralone-1-C^{14} oxime crystallized out. For a more complete separation, the solution was diluted with 150 ml of water (50 ml every 24 hours) before removal of the oxime. The yield of α-tetralone-1-C^{14} oxime with m.p. 98-100° was 12.77 g. According to literature data, α-tetralone oxime has m.p. 103° [24]. Evaporation of the methyl alcohol from the mother liquor yielded an additional amount of oxime, which was purified by recrystallization from aqueous methyl alcohol. The yield was 1.05 g and the m.p. 92-95°.

The total yield of α-tetralone-1-C^{14} oxime was 92.8% (on the initial cyanide).

1-Naphthylamine-1-C^{14} hydrochloride. 10.5 ml (111 mmoles) of acetic anhydride was added to a solution of 13.65 g (84.7 mmoles) of α-tetralone-1-C^{14} oxime in 86 ml of 99.8% acetic acid (solidification point 16.3°), prepared in a flask fitted with a reflux condenser and a bubbler tube. After 1-1.5 minutes the whole mixture

* The analysis was carried out by Liebig's method [22].

thickened due to the liberation of crystals of the acetyl derivative of the oxime. When the temperature of the bath was raised to 100° over 2 hours, the acetyl derivative of the oxime dissolved, giving a solution which gradually acquired a red violet color. The reaction mixture was kept for 2.5 hours with the bath temperature at 102-108°, while a stream of dry hydrogen chloride was passed through the bubbler. During this time, crystals of 1-naphthylamine-1-C^{14} hydrochloride separated from the solution. (Crystals of the hydrochloride periodically stopped up the bubbler tube; to remove the "plug" formed, we used a glass rod set in a rubber seal in the bubbler tube.) A condenser with a Claisen head was connected to the flask and the acetic acid carefully distilled off from the suspension obtained in vacuum (bath temperature 80°). The residue was treated with 120 ml of hydrochloric acid (1 : 1), heated on a bath to 140-145° (the crystalline precipitate then dissolved) and kept at this temperature for 7.5 hours. On cooling, the solution, whose surface was covered with a small layer of a viscous oil, deposited a yellowish crystalline precipitate of 1-naphthylamine-1-C^{14} hydrochloride.

To remove tarry materials from the hydrochloride, the mixture obtained was shaken with 60 ml of chloroform for several minutes. After this, the 1-naphthylamine-1-C^{14} hydrochloride was filtered off, washed three times with 15-ml portions of chloroform and dried in vacuum over calcium chloride. The slightly grey, crystalline product was obtained in a yield of 7.60 g (49.8%). Analysis by diazotization of samples, obtained in model experiments, showed that 1-naphthylamine hydrochloride content of similar preparations was 95-98%.

After separation of the chloroform, the aqueous layer was washed with benzene and then extracted with ether after being made alkaline with a 20% solution of sodium hydroxide. The ether extract was dried over potassium hydroxide and then treated with dry hydrogen chloride to give a further 0.30 g (2.0%) of 1-naphthylamine-1-C^{14} hydrochloride.

Extraction of the red-brown chloroform layer with 10% sodium hydroxide solution yielded 2.06 g (16.8%) of a mixture of 1- and 2-naphthols with m.p. 106-109°.

1-Chloronaphthalene-1-C^{14}. 3.80 g (21.1 mmoles) of 1-naphthylamine-1-C^{14} hydrochloride, 70 ml of water and 1 ml of concentrated hydrochloric acid was heated until the precipitate completely dissolved, 25 ml of concentrated hydrochloric acid added and the solution then quickly cooled. The suspension of 1-naphthylamine-1-C^{14} hydrochloride was cooled to −13°, 4.70 ml of 4.38 N sodium nitrite solution (20.7 mmoles) added (beneath the liquid layer) and the mixture stirred for a further hour while the temperature was kept at from −9 to −12°. The brown solution of the diazo compound was filtered through a porous glass filter (No. 2), cooled in an ice-salt mixture, and added to a freshly prepared hydrochloric acid solution of cuprous chloride (prepared from 5.30 g of copper sulfate by reduction with bisulfite [25] followed by solution in 8 ml of concentrated hydrochloric acid), cooled to 0°. The suspension obtained was placed in a flask with a reflux condenser, heated to 80° (bath temperature) and kept with periodic shaking at 80° for 30 minutes and at 100° for 30 minutes. During this time the evolution of nitrogen completely ceased. The 1-chloronaphthalene-1-C^{14} formed during the reaction was steam distilled off. The distillate was extracted with ether; the ether extract was washed with dilute sodium hydroxide solution and dried with calcium chloride. After evaporation of the ether, the residual oil was distilled from a 10-ml Claisen flask (height of pear column, 5 cm). The 1-chloronaphthalene-1-C^{14} obtained in this way was an almost colorless liquid with b.p. 98-100° (5 mm) and the yield was 1.68 g (49.3%). According to literature data, the boiling point of 1-chloronaphthalene is 104.8° at 5 mm [25]. Into the Claisen flask was placed 2.35 g of inactive 1-chloronaphthalene* and the vacuum distillation repeated. The 1-chloronaphthalene distilled off (2.30 g, b.p. 98-99° at 5 mm) and a further 2.80 g of an inactive preparation was added to the radioactive sample. The 1-chloronaphthalene-1-C^{14} preparation obtained in this way had solid. point −3.8° (according to literature data [6], the solid. point of 1-chloronaphthalene is −2.3°).

Isomerization of 1-chloronaphthalene-1-C^{14} and isolation of 2-chloronaphthalene. The catalysis tube 1 (Fig. 2), made from heat resistant glass (internal diameter 12 mm), had a heating spiral (on top of a layer of asbestos) on the working section with coils arranged so that the variation in temperature along the tube did not exceed 10°. A layer of catalyst (180 mm high) was placed in tube 1 between two layers of broken porcelain; the upper of these (10 mm high) was used to evaporate the 1-chloronaphthalene-1-C^{14}. As the catalyst for the isomerization we used granulated synthetic aluminosilicate catalyst for cracking petroleum.

The 1-chloronaphthalene-1-C^{14} was fed from reservoir 2 into tube 1 by means of compressed air, produced

* The preparation was obtained by recrystallizing distilled technical 1-chloronaphthalene (solid. point −8°) 5 times from anhydrous alcohol at −60° and had b.p. 121° (13 mm) and solid. point −3.3°.

by moving plunger 3. A steady input was thus achieved by maintaining a constant pressure. The end of capillary 4 leading into the catalysis tube 2 was pulled out (however, without reducing the internal diameter of the capillary). This made it possible to reduce the weight of a drop of 1-chloronaphthalene-1-C^{14}, supplied to the evaporation zone, to 6-7 mg. The input rate of hydrogen chloride was controlled with the rheometer 6.

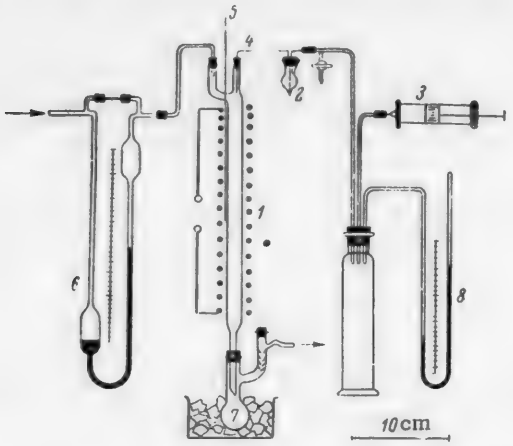


Fig. 2. Apparatus for isomerization of 1-chloronaphthalene-1-C^{14}. 1) Tube with catalyst; 2) reservoir for 1-chloronaphthalene-1-C^{14}; 3) cylinder with plunger; 4) capillary; 5) thermocouple; 6) rheometer; 7) catalyzate receiver; 8) manometric tube.

To remove water contained in the catalyst, tube 1, filled with catalyst, was heated to 250°, while a stream of air was passed through it. Then the stream of air was replaced by a stream of hydrogen chloride, the temperature was raised to 360° over 1 hour and the addition of 1-chloronaphthalene-1-C^{14} begun. The catalyzate was collected in the ice-cooled flask 7.

Experiment 1. The amount of catalyst was 9.45 g. The temperature inside tube 1 was 355-360° (thermocouple 5, placed under the layer of asbestos, was previously calibrated against the readings of a thermometer placed in tube 1). 2.25 g of 1-chloronaphthalene-1-C^{14} was passed through the catalyst over 55 minutes with a hydrogen chloride input rate of 18-20 ml/min (molar ratio 1-$C_{10}H_7Cl$-1-C^{14} : HCl = = 1 : 3.4). This yielded 2.00 g (89%) of a light yellow catalyzate with solidification point 24.7°. This solidification point corresponded to a 2-chloronaphthalene content of 56% [6].

Experiment 2. 3.68 g of 1-chloronaphthalene-1-C^{14} was passed through 9.00 g of catalyst at 360-365° over 85 minutes. The hydrogen chloride input rate was 20 ml/min (molar ratio 1-$C_{10}H_7Cl$-1-C^{14} : HCl = 1 : 3.4). The yield of catalyzate was 3.46 g (94%) and the solid. p. 23.7° (55% 2-chloronaphthalene).

The catalyzates obtained in experiments 1 and 2 were cooled to 0° and the crystalline 2-chloronaphthalene filtered off. The filtered liquid mixture of chloronaphthalenes was dissolved in 7.5 ml of anhydrous alcohol and cooled to −40°. The 2-chloronaphthalene thus precipitated was filtered off and washed with 0.7 ml of anhydrous alcohol, cooled to −40°. This operation was performed 5 more times with the cooling temperature gradually lowered to −70°. A total of 2.58 g of 2-chloronaphthalene was isolated. After recrystallization from a mixture of 12 ml of methyl alcohol and 1 ml of water, the 2-chloronaphthalene appeared as lustrous, colorless plates; yield 1.78 g, m.p. 53-54°. According to literature data the melting point of 2-chloronaphthalene is 61° [27].

2-Naphthol. Into a hermetically sealable stainless steel tube of 26.5 ml capacity was placed 0.68 g (4.2 mmoles) of 2-chloronaphthalene and 16.2 ml (12.9 mmoles) of 0.8011 N sodium hydroxide solution. The tube was placed in a rotating autoclave, which was $^1/_3$ filled with water, heated to 365° over 1 hour and kept at that temperature for 40 minutes. The cooled contents of the tube were filtered and acidified with 5 ml of concentrated hydrochloric acid. This yielded 0.48 g (79.5%) of 2-naphthol with m.p. 106-110°.

Similarly, we obtained 0.72 g (73.8%) of 2-naphthol from the remaining 1.10 g of 2-chloronaphthalene.

Model experiments showed that the nitrosation of 2-naphthol of this nature led to considerable tar formation. Therefore the radioactive 2-naphthol obtained was recrystallized from 140 ml of water. The colorless, lustrous plates (0.74 g yield) had m.p. 119.5-120.5°. A melting point of 122-123° is reported in the literature [28].

1-Nitroso-2-naphthol. To a cooled solution of 0.74 g (5.13 mmoles) of 2-naphthol in 9.0 ml of 0.5740 N sodium hydroxide solution (5.16 mmoles) was added a solution of 0.370 g of 95.5% sodium nitrite (5.13 mmoles) in 4.55 ml of water. The mixture was stirred very vigorously and kept at −0.5 to −1.0°, while 3.35 ml of 2 N sulfuric acid solution was added over 2.5 hours and then stirring was continued for a further 1 hour. The 1-nitroso-2-naphthol obtained was filtered off, washed with water until neutral to congo and dried in vacuum. The yield

was 0.85 g (96%) and the m.p. 101-104°. According to literature data, 1-nitroso-2-naphthol has m.p. 106° [8].

Cis-o-cyanocinnamic acid. A solution of 0.735 g (18.4 mmoles) of sodium hydroxide in 7.6 ml of water was added to a solution of 0.85 g (4.9 mmoles) of 1-nitroso-2-naphthol and 1.86 g (9.8 mmoles) of p-toluenesulfonyl chloride in 16 ml of toluene heated to 70°. The temperature rose to 90° and the reaction mixture boiled. The boiling was maintained for 15 minutes more and then the dark brown reaction mass was quickly cooled. The alkaline layer was separated and the organic layer extracted three times with 10% sodium hydroxide solution (3 ml portions). On acidifying the filtered alkaline solution, we obtained 0.56 g (66%) of cis-o-cyanocinnamic acid with m.p. 132-134°. Recrystallization from 10 ml of water with charcoal added yielded 0.47 g of acid with m.p. 135-136°. According to literature data, the m.p. of cis-o-cyanocinnamic acid is 137° [9].

Trans-o-carbamidocinnamic acid. A mixture of 0.47 g of cis-o-cyanocinnamic acid, 0.44 ml of concentrated hydrochloric acid and 4.8 ml of water was heated for 35 hours under reflux with a bath temperature of 94-96°. During this time the solution gradually deposited crystals of trans-o-carbamidocinnamic acid, which was filtered off through a steam-heated funnel at the end of the reaction. The yield was 0.33 g (63.5%) and the m.p. 231-232° (with gas evolution). Reprecipitation from a 5% soda solution (with charcoal) yielded 0.31 g of a colorless crystalline product with m.p. 236-237°. According to literature data the m.p. is 239° [10].

Found %: C 62.18, 62.14. $C_{10}H_9O_3N$. Calculated %: C 62.81.

Activity: 1987, 2025 μC/ mole.

Trans-o-aminocinnamic acid. A solution of sodium hypobromite, prepared from 0.234 g (1.52 mmoles) of bromine and 1.50 ml of 2.165 N sodium hydroxide solution (3.24 mmoles) was added over 10 minutes to an ice--cooled solution of 259 mg (1.355 mmoles) of trans-o-carbamidocinnamic acid in 2.38 ml of carbonate-free 2.165 N sodium hydroxide solution (5.16 mmoles) and 3 ml of water in flask 1 (Fig. 3).

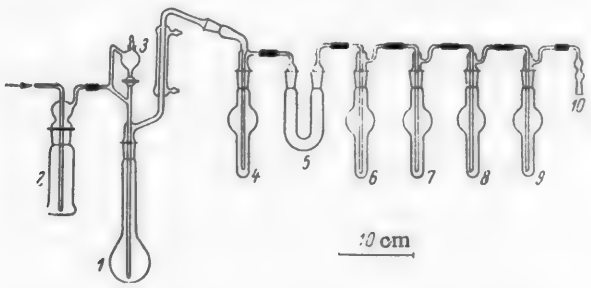


Fig. 3. Apparatus for degradation of trans-o-carbamidocinnamic acid. 1) Reaction flask ; 2) control wash bottle with barium hydroxide solution; 3) dropping funnel; 4) wash bottle with concentrated sulfuric acid; 5) U-tube filled with pieces of pumice impregnated with anhydrous copper sulfate; 6, 7, 8, 9) traps with barium hydroxide solution, 10) tube with ascarite.

The solution was mixed by bubbling through a stream of air, freed from CO_2 by two traps with ascarite. (The absence of CO_2 was checked by the transparency of the barium hydroxide solution in bottle 2). The reaction mixture was kept at 0° for 10 minutes, heated to boiling over 3 hours and boiled for 15 minutes. Air was passed through continuously and the traps 6-9 were filled with 15, 10, 10 and 10 ml respectively of 0.2570 N barium hydroxide solution containing 20 g of barium chloride per liter. To the ice-cooled, dark orange solution in flask 1 was gradually added 3.7 ml of 2.165 N hydrochloric acid from funnel 3. The carbon dioxide thus liberated was flushed through with a stream of air and absorbed in traps 6-9. The U-tube 5, filled with pieces of pumice impregnated with anhydrous copper sulfate, was used to absorb hydrogen chloride flushed out of flask 1 with the air [29].

5.5 liters of air was passed through over a period of 3 hours. The transparency of the solution in trap 9 confirmed the completeness of CO_2 absorption. The amount of carbon dioxide absorbed in the first three traps was determined by titrating the excess barium hydroxide with 0.1 N hydrochloric acid solution. The consumption of

the latter was 62.80 ml, which corresponds to 1.357 mmoles (100.2%) of CO_2. The activity of the barium carbonate obtained was 1855 μC/ mole. The solution in flask 1 was treated with sodium hydroxide solution until weakly acid to congo and extracted 8 times with ether. The ether extract was dried with baked sodium sulfate and treated with dry hydrogen chloride to give 196 mg (72.5%) of the colorless hydrochloride of trans-o-aminocinnamic acid, which was exactly neutralized with 0.5 N sodium hydroxide solution to yield 120 mg of lemon-yellow trans-o-aminocinnamic acid with m.p. 151.5-152°. According to literature data [10] the m.p. is 158°.

Found %: C 65.70. $C_9H_9O_2N$. Calculated %: C 66.23.

Activity 124.5 μC/ mole.

After recrystallization from 4 ml of water the trans-o-aminocinnamic acid had m.p. 153.5-154.5°.

Found %: C 65.62. Activity 125.5 μC/ mole.

SUMMARY

1. A method was developed for the degradation of 2-chloronaphthalene, which made it possible to eliminate the carbon atom from position 1 as CO_2. The method is also applicable to other 2-substituted naphthalenes which can be converted into 2-naphthol.

2. We synthesized 1-naphthylamine-1-C^{14} and 1-chloronaphthalene-1-C^{14}, which have not been described previously.

3. In the catalytic isomerization of 1-chloronaphthalene-1-C^{14} at 355-365° the chlorine was mainly transferred to position 2 (by 93.8%). This excludes (under the given conditions) an intermolecular mechanism for the isomerization of monochloronaphthalenes with the intermediate formation of naphthalene.

4. A mechanism was proposed for the intermolecular isomerization of monochloronaphthalenes which assumed the intermediate formation of halonium ions.

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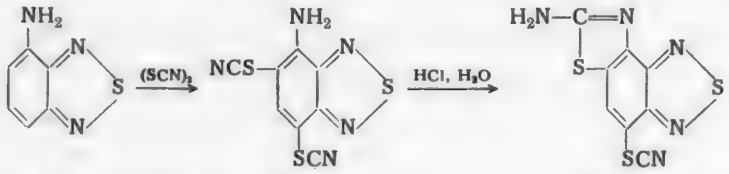
INVESTIGATIONS IN THE FIELD OF 2,1,3-THIODIAZOLE CHEMISTRY

VII. THIOCYANATION OF 4- AND 5-AMINOBENZ-2,1,3-THIODIAZOLES

V. G. Pesin and A. M. Khaletskii

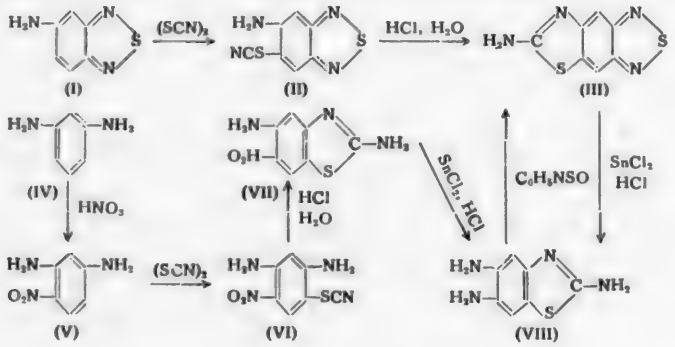
In a previous report [1] we showed that chlorination and bromination of 4-aminobenz-2,1,3-thiodiazole gave 4-amino-5,7-dihalobenz-2,1,3-thiodiazoles; chlorination and bromination of 5-aminobenz-2,1,3-thiodiazole gave, however, 5-amino-6-halobenz-2,1,3-thiodiazoles. Thiocyanation proceeded completely analogously. Thus, thiocyanation of 4-aminobenz-2,1,3-thiodiazole gave a dithiocyano derivative, which was, most probably, 5,7-dithiocyanobenz-2,1,3-thiodiazole, which was converted to a benzthiazole derivative by heating with dilute hydrochloric acid.



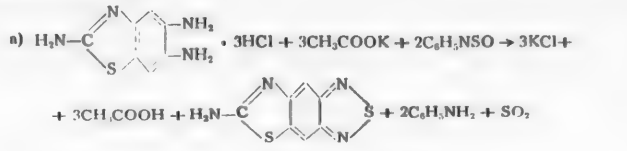
The high reactivity of 4-aminobenz-2,1,3-thiodiazole in halogenation (chlorination, bromination) was particularly well expressed during thiocyanation and the reaction proceeded mainly to form disubstituted derivatives. On reacting equimolecular amounts of the starting materials, part of the 4-aminobenz-2,1,3-thiodiazole did not react; the dithiocyano derivative was formed in approximately 45% yield. When the reactant ratio was calculated so as to give a dithiocyano derivative, the latter was formed in high yield.

Thiocyanation of 5-aminobenz-2,1,3-thiodiazole (I) gave a 6-thiocyano derivative (II), which was isomerized by heating with dilute hydrochloric acid to 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole (III), whose structure was proved by synthesis. For this purpose, m-phenylenediamine (IV) was converted to 4-nitro-1,3-diaminobenzene (V), from which 6-thiocyano-4-nitro-1,3-diaminobenzene (VI) was synthesized by thiocyanation. The latter was isomerized to 2,5-diamino-6-nitrobenzthiazole (VII), which was reduced to 2,5,6-triaminobenzthiazole (VIII), a product identical to that obtained by the reductive decomposition of 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole (III).

Condensation of (VIII) with thionylaniline gave 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole (III), which was identical to the isomerization product of 5-amino-6-thiocyanobenz-2,1,3-thiodiazole (II).

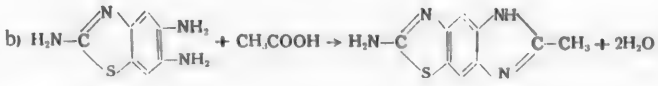


The synthesis of 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole (III) by reacting the hydrochloride of 2,5,6-triaminobenzthiazole with thionylaniline in the presence of potassium acetate, i.e. under conditions of benzimidazole ring formation, indicated that the thiodiazole ring closed very rapidly in comparison with the benzimidazole ring, i.e. the rate of reaction (a)



a) H_2N-C (N, S; $-NH_2$, $-NH_2$) $\cdot 3HCl + 3CH_3COOK + 2C_6H_5NSO \rightarrow 3KCl +$

$+ 3CH_3COOH + H_3N-C$ (N, N, S, S, N) $+ 2C_6H_5NH_2 + SO_2$



b) H_2N-C (N, S; $-NH_2$, $-NH_2$) $+ CH_3COOH \rightarrow H_2N-C$ (N, S; NH, $C-CH_3$, N) $+ 2H_2O$

exceeded that of reaction (b).

As is known, o-aminothiocyano derivatives are extremely unstable and, as a rule, are isomerized to the corresponding 2-aminobenzthiazole derivatives at the moment of formation or during isolation or storage. However, the o-aminothiocyano derivatives of benz-2,1,3-thiodiazole were stable and did not change even when boiled with alcohol or benzene; they were isomerized only by heating with dilute hydrochloric acid or with water. Thus, the thiodiazole ring retarded to a certain degree the intermolecular reaction of the amino and thiocyano groups.

Thiocyanation was carried out (by Kaufmann's method [2]) with thiocyanogen, which was formed by the reaction of bromine with ammonium (potassium) thiocyanate in the presence of ammonium (potassium) bromide in an inert solvent medium (methanol) at 0–2°.

EXPERIMENTAL

4-Amino-5,7-dithiocyanobenz-2,1,3-thiodiazole. 5 g of 4-aminobenz-2,1,3-thiodiazole, m.p. 68°, 16 g of ammonium thiocyanate and 100 ml of methyl alcohol was cooled to 0° and a solution of 12 g of bromine in 115 ml of methyl alcohol, saturated with ammonium bromide, was added at this temperature with continuous stirring over a period of 2.5 hours. The reaction mixture was stirred for 4 more hours and left overnight. The precipitate formed was filtered off and washed with methyl alcohol and water to yield 8.45 g of yellow crystals, which melted at 181° after recrystallization; the yield was 96%.

Found %: C 36.60, 36.43; H 1.52, 1.42; N 26.16, 26.05. $C_8H_3N_5S_3$. Calculated %: C 36.23; H 1.13; N 26.41.

7-Thiocyano-4,5-(2'-aminothiazole)-benz-2,1,3-thiodiazole. A mixture of 0.5 g of 4-amino-5,7-dithiocyanobenz-2,1,3-thiodiazole, 100 ml of water and 1.1 ml of 8% hydrochloric acid was boiled for 5 hours, then cooled and neutralized with sodium bicarbonate and the precipitate filtered off and washed with water. We obtained 0.47 g of yellow crystals with m.p. 178-180°, which were boiled with a mixture of 100 ml of water and 8 ml of concentrated hydrochloric acid for 6 hours and the precipitate filtered off and washed with water; this yielded 0.45 g of yellow crystals, which did not melt at 290° and decomposed when heated further. The crystals either did not dissolve or had very low solubility in organic solvents (ether, alcohol, chloroform etc.).

5-Amino-6-thiocyanobenz-2,1,3-thiodiazole (II). 10 g of 5-aminobenz-2,1,3-thiodiazole (I), m.p. 116°, 300 ml of methyl alcohol and 16 g of ammonium thiocyanate was cooled to 0° and a solution of 11.75 g of bromine in 220 ml of methyl alcohol, saturated with ammonium bromide, was added at this temperature with continuous stirring over 4.5 hours. The reaction mixture was then stirred for 3 hours at 0° and left overnight. The precipitate formed was filtered off and washed successively with methyl alcohol and water; we obtained 11.3 g of yellow crystals with m.p. 179-182°, which solidified after melting and melted again at 257-259°. After recrystallization from benzene the crystals had m.p. 188°. The residue from evaporating the methyl alcohol filtrate to dryness was treated with water, filtered and washed with water and 1.3 g of the material was boiled with 10% hydrochloric acid (in the presence of charcoal) for 1 hour, the hot solution filtered and the hot filtrate made alkaline with 25% ammonia solution. The precipitate formed was filtered off and washed with water; we obtained 1.15 g of crystalline benzthiazole derivative (III) (m.p. 260-262°) in 89% total yield.

Found %: N 26.71, 27.46; S 29.96, 29.93. $C_7H_4N_4S_2$. Calculated %: N 27.00; S 30.77.

5,6-(2'-Aminothiazole)-benz-2,1,3-thiodiazole (III). a) 5.6 g of 5-amino-6-thiocyanobenz-2,1,3-thiodiazole (II) was boiled for 2 hours with 125 ml of concentrated hydrochloric acid and 375 ml of water in the presence of charcoal. The hot solution was filtered and excess 25% NH_4 solution was added to the hot filtrate. The precipitate formed was filtered off and washed with water; we obtained 5.3 g of light yellow crystals with m.p. 262°. A second solution in boiling dilute hydrochloric acid, precipitation with ammonia and recrystallization from dilute dioxan (3 : 1) raised the m.p. to 264°.

Found %: N 26.62. 26.86; S 29.92, 30.17. $C_7H_4N_4S_2$. Calculated %: N 27.00; S 30.77.

b) To a mixture of 1.2 g of 2,5,6-triaminobenzthiazole, 1.5 g of potassium acetate and 15 ml of alcohol was added 2.5 ml of thionylaniline, b.p. 198-200°. The reaction mixture was heated for 30 minutes on a boiling water bath and cooled and the precipitate filtered off and washed successively with alcohol and water. We obtained 0.3 g of green crystals with m.p. 260-261°, which did not depress the melting point of an authentic sample. Boiling with dilute hydrochloric acid (in the presence of charcoal) and subsequent precipitation with ammonia solution raised the m.p. to 264°.

2,5,6-Triaminobenzthiazole hydrochloride (VIII). a) A solution of 22.5 g of stannous chloride in 25 ml of concentrated hydrochloric acid was added over a period of 1.5 hours to 5 g of 5,6-(2'-aminothiazole)-benz-2,1,3--thiodiazole (III) and 25 ml of hydrochloric acid (d 1.19), which was heated on a boiling water bath and stirred. After 3 hours heating and subsequent cooling, the precipitate was filtered off and washed with concentrated hydrochloric acid. We obtained 6 g of a substance which did not melt on heating to 250-260° but acquired a violet color at this temperature and was soluble in water. For purification, 0.6 g of the hydrochloride was boiled for 15 minutes with 7 ml of concentrated hydrochloric acid and 9 ml of water in the presence of charcoal and then the mixture was filtered hot. To the warm colorless filtrate was added 17 ml of concentrated hydrochloric acid and the fine needles which separated were filtered off and washed with concentrated hydrochloric acid.

Found %: N 19.26, 18.99; Cl 37.11, 36.85. $C_7H_{11}N_4SCl_3$. Calculated %: N 19.34, Cl 36.78.

b) Over a period of 30 minutes 14.8 g of stannous chloride in 25 ml of concentrated hydrochloric acid was added with vigorous stirring to 4 g of 2,5-diamino-6-nitrobenzthiazole in 20 ml of hydrochloric acid (d 1.19) at 100°. The reaction mixture was then heated on a boiling water bath for 3 hours and cooled and the precipitate filtered off, washed with concentrated hydrochloric acid and dried. We obtained 6 g of crystals, which were purified by boiling for ½ an hour with a mixture of 40 ml of concentrated hydrochloric acid, 60 ml of water and charcoal; the hot solution was filtered and to the cooled filtrate was added 100 ml of concentrated hydrochloric acid; we obtained 4.7 g of white crystals.

Found %: N 18.92, 18.78; Cl 36.72, 36.78. $C_7H_{11}N_4SCl_3$. Calculated %: N 19.34; Cl 36.78.

4-Nitro-1,3-diaminobenzene (V) was prepared according to literature data [3, 4] by nitration of 1,3-diacetylaminobenzene with subsequent hydrolysis of the 4-nitro-1,3-diacetylaminobenzene.

4-Nitro-6-thiocyano-1,3-diaminobenzene (VI). Over a period of 5 hours, 23.85 g of bromine in 300 ml of methanol saturated with ammonium bromide was added to 20 g of 4-nitro-1,3-diaminobenzene, m.p. 157-159°, 32.6 g of ammonium thiocyanate and 300 ml of methanol stirred vigorously at 0°. After being stirred for 1 hour and left overnight, the precipitate formed was filtered off, washed with methanol and water and dried; we obtained 23.65 g of substance with m.p. 175-176°.

After diluting the filtrate with water and separating the precipitate formed, we obtained a further 5 g of substance with m.p. 143-165°. The substance consisted of crystals which were insoluble in water and readily soluble in many organic solvents and crystallized readily from aqueous alcohol or aqueous acetone; however, the crystals isolated after recrystallization from aqueous alcohol had different properties. Apparently, some kind of conversion had occurred. Heating with dilute hydrochloric acid yielded the corresponding benzthiazole derivative, which we used for purification.

2,5-Diamino-6-nitrobenzthiazole (VII). 5 g of 4-nitro-6-thiocyano-1,3-diaminobenzene, m.p. 175-176°, 700 ml of water and 50 ml of concentrated hydrochloric acid was boiled for 1.5 hours in the presence of charcoal, after which the hot solution was filtered and the filtrate made alkaline with ammonia solution. The orange crystals formed were filtered off and washed with water; we obtained 4.1 g of substance. For analysis, 0.6 g of

this substance was again heated with dilute hydrochloric acid (in the presence of charcoal); the hot solution was made alkaline with ammonia solution and the precipitate formed filtered off and washed successively with water and alcohol.

Found %: C 39.91, 40.37; H 3.10, 3.01; N 26.47, 26.43. $C_7H_6O_2N_4S$. Calculated %: C 40.00; H 2.86, N 26.67.

SUMMARY

1. It was found the thiocyanation of 4-aminobenz-2,1,3-thiodiazole gave a high yield (95%) of 4-amino--5,7-thiocyanobenz-2,1,3-thiodiazole, which was converted to (supposedly) 7-thiocyano-4,5-(2'-aminothiazole)--benz-2,1,3-thiodiazole by heating with dilute hydrochloric acid.

2. It was found that thiocyanation of 5-aminobenz-2,1,3-thiodiazole gave a high yield (90%) of 5-amino--6-thiocyanobenz-2,1,3-thiodiazole, which isomerized to 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole when heated with dilute hydrochloric acid.

3. It was found that thiocyanation of 4-nitro-1,3-diaminobenzene gave, in almost quantitative yield, 6--thiocyano-4-nitro-1,3-diaminobenzene, which isomerized to 2,5-diamino-6-nitrobenzthiazole when heated with dilute hydrochloric acid.

4. A practical method for synthesizing 2,5,6-triaminobenzthiazole in high yield was found.

5. It was shown that the hydrochloride of 2,5,6-triaminobenzthiazole reacted with thionylaniline (in the presence of potassium acetate) to form 5,6-(2'-aminothiazole)-benz-2,1,3-thiodiazole.

6. It was shown that under identical conditions, the thiodiazole ring formed much more readily than the imidazole ring.

7. The reaction of thionylaniline with o-diamines of the aromatic series was extended to include o-diamines of the benzthiazole series, containing an amino group in position 2; in addition, it was shown that o-diamines are capable under certain conditions of reacting with thionylaniline not only as free bases, but also as salts.

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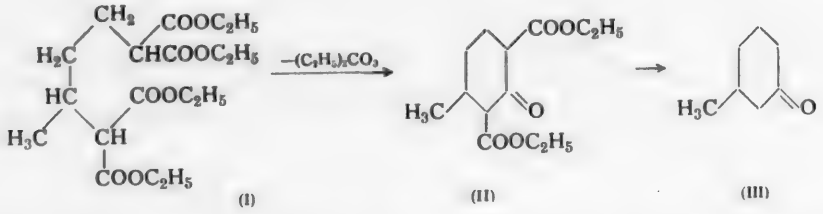
INVESTIGATION IN THE FIELD OF THE DIECKMANN REACTION

IV. CYCLIZATION OF THE TETRAETHYL ESTER OF 2-METHYLPENTANETETRACARBOXYLIC-1,1,5,5 ACID

V. I. Zaretskii and N. S. Vul'fson

In continuing the study of the Dieckmann reaction [1], we investigated the cyclization of the tetraethyl ester of 2-methylpentanetetracarboxylic-1,1,5,5 acid (I). It was found that no cyclization of the tetraester (I) occurred in the presence of sodium powder in benzene (the starting tetraester was recovered), but cyclization did occur in the presence of sodium ethylate in an alcohol solution to give a 44.5% yield of 3-methyl -2,6-dicarbethoxy-cyclohexanone (II). The cyclization was accompanied by the elimination of diethyl carbonate [2,3], which was isolated during the distillation of the reaction product.



(I) (II) (III)

The structure of the ketodiester (II) was confirmed by data from elementary analysis, molecular refraction and its hydrolysis and subsequent decarboxylation to give 3-methylcyclohexanone (III), whose constants agreed with those described in the literature for this substance [4, 6]. The starting tetraethyl ester of 2-methylpentane-tetracarboxylic-1,1,5,5 acid (I) was prepared by condensing 1,3-dibromobutane with sodiomalonic ester. Reaction of stoichiometric amounts of malonic ester and dibromide gave a 12.8% yield of tetraester (I), although 90% of sodium bromide was obtained. By condensing 1 mole of 1,3-dibromobutane with 2 moles of sodiomalonic ester in the presence of a large excess of malonic ester (4 moles) and carrying out the reaction in analogy with the method used by V. P. Gol'mov and B. A. Kazanskii [7], we obtained a 36.9% yield of tetraester (I). A greater excess of malonic ester did not affect the yield of the condensation product.

EXPERIMENTAL

Butanediol-1,3 was prepared by the hydrogenation of technical acetaldol in methanol solution by Hancock's method [8]; the yield, calculated on acetaldehyde, was 36%.

B.p. 80-82° at 2 mm, $n^{20}D$ 1.4415, d^{20}_4 1.0074. According to literature data: b.p. 208-209° at 760 mm, $n^{20}D$ 1.441, d^{20}_4 1.0046 [9].

1,3-Dibromobutane was prepared by the method of Kazanskii and Lukina [10]; the yield was 70%.

B.p. 60-62° at 12 mm, $n^{20}D$ 1.5095, d^{20}_4 1.8062. According to [10]: b.p. 174.5-175.5° at 760 mm, $n^{20}D$ 1.5092, d^{20}_4 1.7904.

Tetraethyl ester of 2-methylpentanetetracarboxylic-1,1,5,5 acid (I). To a solution of sodium ethylate (from 10 g of metallic sodium and 300 ml of anhydrous alcohol) was added 215 g of malonic ester, the solution heated to boiling and stirred and 48 g of dibromobutane-1,3 added to the boiling mass over a period of 2 hours. After

the addition of the dibromide, the mass was boiled till it gave a neutral reaction to moist phenolphthalein paper (9-10 hours). The alcohol was distilled off on a boiling water bath (at the end in a vacuum of about 60 mm) and the residue (a suspension) cooled to room temperature, diluted with 200 ml of water and made weakly acid to congo with 25% sulfuric acid. (I) was extracted with ether (2 × 100 ml), the ether extract washed with water until neutral to congo and dried with anhydrous sodium sulfate, the solvent distilled off and the residue vacuum distilled. We obtained 30.5 g (36.9%) of the tetraester (I) as a slightly yellowish oily liquid.

B.p. 186-192° at 3.5 mm, $n^{20}D$ 1.4450, d^{20}_4 1.0883, MR_D 92.74; calc. for keto form 91.94, for enol form 94.034.

Found %: C 57.80; H 7.96. $C_{18}H_{30}O_8$. Calculated %: C 57.75; H 8.02.

Cyclization of tetraethyl ester of 2-methylpentanetetracarboxylic-1,1,5,5 acid (I). To a solution of sodium ethylate (from 16.8 g of sodium and 350 ml of anhydrous alcohol) was added 168.6 g of the tetraester (I) and the solution stirred and boiled for 3 hours. The alcohol was distilled off on a boiling water bath (at the end in a vacuum of 125-170 mm), the residue poured onto 300 g of ice with external cooling with snow and salt keeping the temperature at from −3 to 0°, 200 ml of ether added and the mixture made acid to congo with dilute sulfuric acid (1 : 4) with the temperature kept at from 0 to 3°. The ether layer was separated, the aqueous layer diluted with 400 ml of water, the reaction product extracted with ether (2 × 150 ml) and the combined ether solutions washed with water (4 × 150 ml), 5% soda solution (3 × 50 ml) and again with water. The extract was dried with anhydrous sodium sulfate, the solvent distilled off and the residue vacuum distilled to give the following fractions: 1st 39° at 200 mm − 45° at 22 mm, 5.5 g; 2nd 116-135° at 2.5 mm, 13.8 g; $n^{20}D$ 1.4620; 3rd 135-140.5° at 2.5 mm, 41.6 g, $n^{20}D$ 1.4710; 4th 140.5-145.5° at 2.5 mm (practically all distilled over at 140.5-142° at 2.5 mm), 17.1 g, $n^{20}D$ 1.4690; residue 23.2 g.

A second distillation of the 1st fraction yielded 1.7 g of diethyl carbonate with b.p. 123-124°, $n^{20}D$ 1.3850; heating with a methanol solution of sodium hydroxide gave a precipitate of Na_2CO_3. According to literature data: b.p. 126°, $n^{20}D$ 1.38456 [11].

The 2nd fraction and the residue were combined and redistilled. This yielded fractions: 1st 66° at 1.5 mm − 133° at 2 mm, 10.3 g, $n^{20}D$ 1.4527; 2'nd 133-143° at 2 mm, 4.8 g, $n^{20}D$ 1.4688; 3'rd 143° at 2 mm − 189° at 2.5 mm, 13.5 g, $n^{20}D$ 1.4570.

The 3'rd fraction apparently contained mainly unreacted tetraester (I), but fractions 3, 4 and 2' consisted mainly of the cyclic ketoester (II); with an aqueous solution of ferric chloride they gave a violet color. These three fractions were combined and again distilled; the following fractions were collected: 1"st 108-119° at 1 mm, 5.9 g, $n^{20}D$ 1.4695; 2"nd 118.5-124.2° at 1 mm, 39.6 g, $n^{20}D$ 1.4720, d^{20}_4 1.0991; 3"rd 124.2-129° at 1 mm, 11.1 g, $n^{20}D$ 1.4705.

Fraction 2": MR_D 64.71, calc. for enol 64.4, for ketone 63.37.

Found %: C 61.30; H 8.05. $C_{13}H_{20}O_5$. Calculated %: C 60.92; H 7.87.

Fraction 3".

Found %: C 61.35; H 8.09. $C_{13}H_{20}O_5$. Calculated %: C 60.92; H 7.87.

Thus, fractions 2" and 3", which were colorless, mobile liquids with an ester smell, were pure 3-methyl-2,6-dicarbethoxycyclohexanone (II).

3-Methylcyclohexanone (III). 62.5 g of potassium hydroxide was dissolved with boiling in 93.5 ml of anhydrous methanol, the hot solution quickly cooled to −4° and 51.1 g of 3-methyl-2,6-dicarbethoxycyclohexanone (II; fraction 2" and 3") added over a period of 20 minutes to the thick mass at a temperature of −4 to 7°, while cooling in ice and salt was continued. The quickly thickening mass was left at 20-22° for 17 days, after which it was dissolved in 200 ml of cold water, acidified with 30% sulfuric acid, a further 50 ml of concentrated sulfuric acid added and the solution steam distilled.

3-Methylcyclohexanone (III) was extracted from the distillate with ether (5 × 100 ml) and the ether solution dried with anhydrous sodium sulfate and distilled; the yield of (III) was 7.8 g (34.9%).

B.p. 164-167.5°, $n^{20}D$, 1.4455, d^{20}_4 0.9127; semicarbazone, m.p. 181-182° (from 70% alcohol). According to literature data: b.p. 165-168°, $n^{21}D$ 1.4450; semicarbazone, m.p. 179° (from CH_3OH) [4], $n^{20}D$ 1.4460; d^{20}_4 0.9155 [5]; d^{20}_4 0.9136; semicarbazone, m.p. 180° [6].

SUMMARY

We studied the cyclization of the tetraethyl ester of 2-methylpentanetetracarboxylic-1,1,5,5 acid by Dieckmann's method. It was shown that the primary reaction product was 3-methyl-2,6-dicarbethoxycyclohexanone and its structure was confirmed by the production of 3-methylcyclohexanone from it by ketonic cleavage.

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REACTIONS OF METAL ALCOHOLATE HALIDES

V. THE MECHANISM OF THE REACTION OF MAGNESIUM CARBINOLATE HALIDES WITH ESTERS

I. I. Lapkin, O. M. LapRina and M. N. Rybakova

Previous investigations [1-3] of magnesium diarylcarbinolate halide reactions with esters of formic acid showed that magnesium diarylcarbinolate halides with unsubstituted ortho-positions form diarylmethyl halides while magnesium diarylcarbinolate halides with all four ortho-positions occupied by methyl groups form hydrocarbons – diarylmethanes. The purpose of this work was to determine the number of ortho-substituents at which hydrocarbons of the diarylmethane type are formed instead of halides.

Investigations carried out with magnesium diarylcarbinolate halides with gradually increasing numbers of ortho-substituents, showed that with less than four substituents this reaction gave diarylmethyl halides. It is possible that diarylmethanes would be formed with three secondary and tertiary radicals, but with more complicated ones than methyl. However, we have not as yet elucidated this problem.

Esters of oxalic acid react with magnesium diarylcarbinolate halides similarly to esters of formic acid. The only difference observed was in relation to magnesium diarylcarbinolate halides with four ortho-positions occupied as the carbinol was regenerated by decomposing the diethyl oxalate reaction products with water and acid.

Examples of malonic ester reactions with magnesium di-o-tolylcarbinolate bromide and with magnesium di-p-tolylcarbinolate bromide confirmed the fact established earlier [1], that, in contrast to esters of formic and oxalic acids, malonic ester formed diarylmethyl ethers with the given carbinolates. The investigation results are given in the table.

The problem of the reaction mechanism of magnesium carbinolate halides with esters arises in connection with the results of the present work and that carried out earlier [1-3]. A solution of this problem would make it possible to forsee new forms of magnesium carbinolate halide reactions and also find an explanation for the nature of many of the anomalies observed in organomagnesium reactions. As is known, G. A. Stadnikov [4] studied the reactions of magnesium alcoholate halides with esters using mainly ethyl acetate. He investigated the reactions of the magnesium alcoholate iodides of benzhydrol, β-methylcyclohexanol and menthol with twice the amount of ethyl acetate and these gave the acetates of the alcohols named. He also established that treatment of ethyl acetate with the magnesium alcoholate iodide of benzhydrol gave dibenzhydryl and benzhydryl ethyl ethers. Stadnikov explained the formation of these ethers and esters in the following way. Organomagnesium compounds react with esters to form first magnesium alcoholate halides of a secondary (if an ester of formic acid is used) or tertiary alcohol. The alcoholate formed reacts with the as yet unreacted starting ester to form the ester of the alcohol synthesized.

$$(R)_2CHOMgI + CH_3COOC_2H_5 \longrightarrow (R)_2CHOCOCH_3 + C_2H_5OMgI$$

According to Stadnikov the ester will then react with magnesium iodide to form an iodide corresponding to the alcohol being synthesized, although Stadnikov did not succeed in isolating an iodide in any of the cases.

$$(R)_2CHOCOCH_3 + MgI_2 \longrightarrow (R)_2CHI + CH_3COOMgI$$

The iodide formed may then lead to three products: 1) reacting with the magnesium alcoholate iodide of the alcohol synthesized, it may give the ether of this alcohol; 2) reacting with the ethylmagnesium iodide found in the reaction mixture, it may give a mixed ester of the alcohol synthesized; and 3) reacting with the unreacted magnesium iodide it may give a hydrocarbon.

According to Stadnikov's data, the above products may be obtained by carrying out the reaction at the boiling point of the ester adding a double quantity of ester, not dropwise, but in one portion and boiling the mixture for many hours (sometimes 40-50 hours).

Reaction components (1 : 1 ratio)	Composition of reaction products (in %)		
	halide	diaryl-carbinol	diarylmethyl ether
MgCl-phenyl-α-naphthylcarbinolate + ethyl formate	86	14	–
MgBr-phenyl-α-naphthylcarbinolate + ethyl formate	88	12	–
MgBr-phenyl-α-naphthylcarbinolate + diethyl oxalate	96	4	–
MgBr-p-xylyl-α-naphthylcarbinolate + ethyl formate	72	28	–
MgBr-di-p-xylylcarbinolate + diethyl oxalate	100	–	–
MgCl-o-tolyl-α-naphthylcarbinolate + ethyl formate	100	–	–
MgBr-o-tolyl-α-naphthylcarbinolate + ethyl formate	100	–	–
MgBr-phenyl-pentamethylphenylcarbinolate + ethyl formate .	100	–	–
MgCl-mesityl-α-naphthylcarbinolate + ethyl formate	100	–	–
MgBr-mesityl-α-naphthylcarbinolate + ethyl formate	100	–	–
MgCl-di-p-tolylcarbinolate + diethyl oxalate	70	30	–
MgBr-di-p-tolylcarbinolate + diethyl oxalate	100	–	–
MgBr-di-p-tolylcarbinolate + diethyl malonate	20	–	80
MgBr-di-o-tolylcarbinolate + diethyl malonate	8	–	92
MgBr-dimesitylcarbinolate + diethyl oxalate	–	100	–

The reasons for the formation of such side products as tetraarylethanes and ethers was established correctly in Stadnikov's scheme; however, we cannot agree with the formation schemes he gives for iodides and esters as, for example, esters (benzhydryl acetate and benzhydryl formate) heated with $MgCl_2$ and $MgBr_2$ in an ether solution do not form a halide although, according to our investigations the latter is readily formed by reacting magnesium benzhydrolate chloride with ethyl formate and ethyl oxalate and no halide is formed on heating benzhydryl ethyl ether with $MgCl_2$ and $MgBr_2$.

As mentioned above, we found the conditions for liberating halides by reacting magnesium diarylcarbinolate halides with esters, and the halide yield depended on the character of both the diarylcarbinols and the esters. We consider the mechanism of the reaction between these substances to be as follows.

As is known, the work by Karasch [5] and A. N. Nesmeianov and K. A. Kochetkov [6] made it possible to establish the order of so-called relative electronegativity of various radicals:

$$CH_3 > C_2H_5 > n\text{-}C_3H_7 > n\text{-}C_4H_9 > n\text{-}C_7H_{15} > iso\text{-}C_3H_7 >$$

$$> (CH_3)_2CH-CH_2-CH_2 > \ldots$$

If this idea is carried over to the alkoxyl groups, then we would be able to predict the following order of relative electronegativity of the alkoxyl groups:

$$CH_3O > C_2H_5O > n\text{-}C_3H_7O- > n\text{-}C_4H_9O > n\text{-}C_7H_{15}O >$$

$$> (CH_3)_2CHO > (CH_3)_2CH-CH_2-CH_2O > \ldots$$

If we consider the electronic characteristics of the groups listed, we can then find the mechanism of the given reaction.

The reaction of magnesium alcoholate halides of aliphatic and alicyclic alcohols with ethyl formate gives an initial product of formula (I), which, when treated with dilute acid, is converted into an ester of ortho-formic acid (II).

(I) $R-OCH(OC_2H_5)(OMgX)$ (II) $R-OCH(OC_2H_5)OH$

As the alkoxyl groups are bonded weakly in acetals and in partial esters of ortho-acids, during the stabilization of this product the most negative alkoxyl group is eliminated in the form of alcohol.

$$R-OCH(OC_2H_5)OH \rightarrow R-O-COH + C_2H_5OH$$

Magnesium alcoholate halides of aliphatic and alicyclic alcohols usually react with esters in this way. The reaction products are esters.

On introducing benzyl or benzylhydryl radicals whose bonds with oxygen are extremely weak, into compound (I), instead of R, compound (I) is stabilized by the following scheme:

$$(C_6H_5)_2CH-O-CH(OC_2H_5)(OMgX) \rightarrow (C_6H_5)_2CHX + CH(OC_2H_5)O_2Mg$$

If alkyl groups, in particular methyl groups, are present in the ortho-position in the phenyl rings, then due to the steric order the halogen cannot migrate to the central carbon atom as the halogens have relatively large atomic volumes. Because of the above, compound (I) is converted by another scheme which results in the formation of a hydrocarbon.

$$[(CH_3)_3C_6H_2]_2CH-O-CH(OC_2H_5)(OMgX) \rightarrow [(CH_3)_3C_6H_2]_2CH_2 + CO(OMgX)(OC_2H_5)$$

The accuracy of this mechanism is confirmed by the fact that when diethyl oxalate is used in the reaction instead of ethylformate, dimesitylmethane could not be formed as hydrogen, capable of migrating to the dimesitylmethyl radical, is absent from the addition product. Therefore, instead of a hydrocarbon being formed, dimesitylcarbinol is again regenerated.

$$[(CH_3)_3C_6H_2]_2CH-O-C(OMgX)(COOC_2H_5)(OC_2H_5) \xrightarrow{H_2O}$$
$$\rightarrow [(CH_3)_3C_6H_2]_2CHOH + CO(OMgX)(COOC_2H_5)$$

The formation of diarylmethyl halides in magnesium diarylcarbinolate halide reactions by the given scheme causes secondary reactions. For example, the formation of symmetrical tetraphenylethane may be explained, doubtlessly, by a Wurtz type of reaction between benzhydryl bromide and metallic magnesium as experimental data indicate [7].

The slow formation of diarylmethyl halides when magnesium diarylcarbinolate halides are heated with diethyl succinate, diethyl malonate or diethyl sulfate results in the formation of ethers. The formation of these compounds may be represented by the usual scheme

$$R_2CHBr + R_2CHOMgBr \rightarrow R_2-CH-O-CHR_2 + MgBr_2$$

It was previously shown [3] that acetone reacted with phenylmagnesium bromide and ethyl benzoate with ethylmagnesium bromide to form magnesium alcoholate bromides of the corresponding tertiary alcohols, which were decomposed by water to tertiary alcohols. If, before decomposing the reaction mixture with water, an equimolecular amount of ethyl formate or ethyl oxalate was added to it, then instead of tertiary alcohols, their dehydration products (unsaturated hydrocarbons) were formed. Such a reaction course is explained by the fact that these esters react with magnesium alcoholate bromides of tertiary aliphatic-aromatic alcohols to form bromides, from which hydrogen bromide is then eliminated and unsaturated hydrocarbons are formed.

Very often deviations from the usual reaction course are observed in reactions of esters with organomagnesium compounds. The mechanism proposed for the reaction of magnesium alcoholate halides with esters makes it possible to explain these anomalies from a single point of view. The appearance of these anomalies is caused by a side reaction between the magnesium alcoholate halides first formed and the esters.

Numerous experiments for studying the reaction of magnesium phenolate halides and magnesium naphtholate halides with esters showed that, in contrast to alcoholates, phenolates and naphtholates do not react with esters.

EXPERIMENTAL*

The reactions between magnesium carbinolate halides and esters were performed under the following conditions. To the diarylcarbinol, dissolved in three volumes of anhydrous ether, was added an ether (3 volumes) solution of the organomagnesium compound, freed from excess magnesium (n-butylmagnesium chloride for the preparation of magnesium carbinolate chlorides and ethylmagnesium bromide for the preparation of magnesium carbinolate bromides). To the ether solution of magnesium carbinolate halide, prepared in this way, was added an equimolecular amount of the ester, dissolved in an equal volume of anhydrous ether. The reaction mixture

* Carried out with the participation of the students L. P. Gladkii, L. I. Akoeva, T. N. Povarnitsina and E. I. Terent'eva.

was heated for 2 hours and decomposed with water and 10% acetic acid. The ether layer was washed with a 10% solution of sodium carbonate and then water until neutral. If ethyl oxalate was used for the reaction, then magnesium oxalate was liberated from the ether layer and precipitated in the aqueous layer. After the ether solution had been dried with baked sodium sulfate, the solvent was distilled off and the product examined after vacuum distillation.

1. Reaction of magnesium phenyl-α-naphthylcarbinolate chloride and bromide with ethyl formate. Starting materials: 6 g ($^1/_{39}$ mole) of phenyl-α-naphthylcarbinol (m.p. 48°), 2.4 g of butyl chloride, 1.9 g of ethyl formate and 1 g of magnesium. Treatment of a sample of the material obtained from the reaction with a saturated solution of silver nitrate in alcohol with heating [8] indicated a chlorine content of 12.06% (calculated for phenyl-α-naphthylmethyl chloride, 14.03%). Consequently the product obtained contained 86% chloride.

The reaction of magnesium phenyl-α-naphthylcarbinolate bromide with ethyl formate was performed with the same amounts of starting materials (ethyl bromide was used instead of butyl chloride) and lead to the formation of phenyl-α-naphthylmethyl bromide in 88% yield (found %: Br 23.66; calc. 26.59).

Substitution of the ethyl formate by diethyl oxalate increased the yield of phenyl-α-naphthylmethyl bromide to 96%.

Found %: Br 25.80. $C_{17}H_{13}Br$. Calculated %: Br 26.89.

2. Reaction of magnesium p-xylyl-α-naphthylcarbinolate bromide with ethyl formate. p-Xylyl-α-naphthylcarbinol (2,5-dimethylphenyl-α-naphthylcarbinol) was synthesized by reacting p-xylylmagnesium bromide with α-naphthaldehyde. The m.p. was 122° (from a mixture of equal volumes of petroleum ether and toluene). The yield was 52%. The material is not described in the literature.

Found %: C 86.72; H 6.88; OH 6.35. $C_{19}H_{18}O$. Calculated %: C 86.98; H 6.92; OH 6.48.

The addition of an ether solution of ethylmagnesium bromide (the ethylmagnesium bromide content of the ether solution was determined by titration with hydrochloric acid solution) to 7.6 g ($^1/_{40}$ mole) of carbinol gave the magnesium carbinolate bromide, to which ethyl formate (1.9 g) was then added. After the usual operations of heating, decomposing the reaction mixture and distilling off the solvent, a sample of the material obtained was heated with a saturated alcohol solution of silver nitrate. The p-xylyl-α-naphthylmethyl bromide content was 72%.

Found %: Br 17.60, $C_{19}H_{17}Br$. Calculated %: Br 24.57.

3. Reaction of magnesium di-p-xylylcarbinolate bromide with diethyl oxalate. Di-p-xylylcarbinol (2,5,2',5'-tetramethylbenzhydrol) was prepared by reacting p-xylylmagnesium bromide with ethyl formate. The m.p. was 144° (from toluene). The yield was 48%. The material is not described in the literature.

Found %: C 84.70; H 8.42; OH 6.5. $C_{17}H_{20}O$. Calculated %: C 84.95; H 8.39; OH 7.1.

Part of the carbinol obtained was converted into the magnesium carbinolate bromide by the addition of a definite amount of an ether solution of ethylmagnesium bromide. Diethyl oxalate was then added to the carbinolate. The other reactionconditions are described above. When the solvent had been distilled off, the di-p-xylylmethyl bromide (not described in the literature) crystallized and was recrystallized from petroleum ether. The m.p. was 95-96°.

Found %: Br 26.17. $C_{17}H_{19}Br$. Calculated %: Br 26.35.

4. Reaction of magnesium o-tolyl-α-naphthylcarbinolate chloride and bromide with ethyl formate. o-Tolyl-α-naphthylcarbinol, which is not described in the chemical literature, was synthesized by the reaction of o-tolylmagnesium bromide with α-naphthaldehyde. The m.p. was 120-121° (from a mixture of petroleum ether and benzene). The yield was 48%.

Found %: C 86.87; H 6.41; OH 6.2. $C_{18}H_{16}O$. Calculated %: C 87.07; H 6.50; OH 6.8.

The carbinol (6.2 g), dissolved in three volumes of anhydrous ether, as described above, was converted into magnesium carbinolate chloride by the addition of an ether solution of butylmagnesium chloride, and then treated with an ether solution of ethyl formate (1.9 g). The o-tolyl-α-naphthylmethyl chloride (not described in the literature) obtained crystallized and was purified by recrystallization from petroleum ether. The m.p. was 91°.

Found %: Cl 13.01. $C_{18}H_{15}Cl$. Calculated %: Cl 13.29.

Under similar conditions and with the same amounts ($^1/_{40}$ of a mole) of starting materials (ethyl bromide was used instead of butyl chloride) magnesium o-tolyl-α-naphthylcarbinolate bromide was reacted with ethyl formate. The only reaction product was o-tolyl-α-naphthylmethyl bromide with m.p. 94° (from petroleum ether, which was obtained for the first time).

Found %: Br 25.21. $C_{18}H_{15}Br$. Calculated %: Br 25.68.

5. Reaction of magnesium mesityl-α-naphthylcarbinolate chloride and bromide with ethyl formate. Mesityl-α-naphthylcarbinol, which has not been described previously, was synthesized by the reaction of mesitylmagnesium bromide with α-naphthaldehyde. The m.p. was 131° (from a mixture of petroleum ether and toluene). The yield was 33%.

Found %: C 86.72; H 7.18; OH 5.8. $C_{20}H_{20}O$. Calculated %: C 86.93; H 7.30; OH 6.1.

The conditions of the reaction of magnesium mesityl-α-naphthylcarbinolate chloride with ethyl formate and also magnesium mesityl-α-naphthylcarbinolate bromide with the same ester are described above. $^1/_{40}$ mole amounts of the materials required for the reaction (carbinol, butyl chloride or ethyl bromide, magnesium and ethyl formate) were used. The only product of the first reaction was mesityl-α-naphthylmethyl chloride, which was obtained for the first time. The m.p. was 98° (from petroleum ether).

Found %: Cl 11.70. $C_{20}H_{19}Cl$. Calculated %: Cl 12.03.

The product of the second reaction was mesityl-α-naphthylmethyl bromide, which also has not been described previously. The m.p. was 100° (from petroleum ether).

Found %: Br 23.25. $C_{20}H_{19}Br$. Calculated %: Br 23.56.

6. Reaction of magnesium 2,3,4,5,6-pentamethylbenzhydrolate bromide with ethyl formate. 2,3,4,5,6-Pentamethylbenzhydrol was prepared by the reaction of pentamethylphenylmagnesium bromide with benzaldehyde. The m.p. was 105°. A m.p. of 107° is reported in the literature [9]. The reaction conditions for magnesium 2,3,4,5,6-pentamethylbenzhydrolate bromide with ethyl formate are described above. Evaporation of the solvent yielded for the first time 2,3,4,5,6-pentamethylbenzhydryl bromide, which crystallized and had a constant m.p. of 98° after recrystallization from petroleum ether.

Found %: Br 24.80. $C_{18}H_{21}Br$. Calculated %: Br 25.19.

7. Reaction of magnesium di-p-tolylcarbinolate chloride and bromide with diethyl oxalate. Di-p-tolylcarbinol was prepared under the normal Grignard conditions by the reaction of p-tolylmagnesium bromide with ethyl formate. The m.p. was 72°. For this carbinol a m.p. of 71° is reported in the literature [10]. The reaction of magnesium di-p-tolylcarbinolate chloride with diethyloxalate was performed as in the previous experiments with $^1/_{40}$ mole amounts of the starting materials. The di-p-tolylmethyl chloride content of reaction product was 70% (found %: Cl 10.80; calc. 15.73). To convert the unreacted carbinol into chloride and to isolate the chloride in a pure form, the reaction product was dissolved in petroleum ether and a stream of dry hydrogen chloride passed through the solution. The di-p-tolylmethyl chloride isolated had m.p. 42° (from petroleum ether).

Found %: Cl 15.52. $C_{15}H_{15}Cl$. Calculated %: Cl 15.73.

In contrast to the magnesium carbinolate chloride, the magnesium di-p-tolylcarbinolate bromide was completely converted into di-p-tolylmethyl bromide by reaction with diethyl oxalate. The m.p. of the product was 49° (from petroleum ether) [11].

Found %: Br 28.73. $C_{15}H_{15}Br$. Calculated %: Br 29.04.

8. Reaction of magnesium di-p-tolylcarbinolate bromide and magnesium di-o-tolylcarbinolate bromide with diethyl malonate. As a result of the first reaction, evaporation of the solvent and the malonic ester residue yielded a product which contained 20% of di-p-tolylmethyl bromide (found %: Br 5.8; calc. 29.04). No carbinol content was found. This product was vacuum distilled. The bulk of the material distilled over in the range 228-238° at 8 mm. Recrystallization from a mixture of petroleum ether and toluene (1 : 1) gave for the first time di-p-tolylmethyl ether with m.p. 186°.

Found %: C 88.41; H 7.35. $C_{30}H_{30}O$. Calculated %: C 88.63; H 7.44.

The second reaction (magnesium di-o-tolylcarbinolate bromide with diethyl malonate) was carried out

similarly to the first and gave the following results: the di-o-tolylmethyl bromide content of the reaction product was 8% (found %: Br 2.3; calc. 29.04); carbinol was not found but there was a 92% content of di-o-tolylmethyl ether, which has not been described previously in the literature. The m.p. of the latter material was 172° (from a mixture of petroleum ether and toluene).

Found %: C 88.39; H 7.30. $C_{30}H_{30}O$. Calculated %: C 88.63; H 7.44.

SUMMARY

1. The study of the reaction of magnesium diarylcarbinolate halides with esters was continued. It was established that only those magnesium diarylcarbinolate halides which have all four ortho-positions occupied by alkyl groups form diarylmethanes with esters of formic acid, while with a lower degree of substitution these reactions give diarylmethyl halides.

2. New examples were used to show that on reaction with malonic esters, magnesium diarylcarbinolate halides are converted to diarylmethyl ethers.

3. It was established that magnesium phenolate bromides and magnesium naphtholate bromides do not react with the esters of formic, oxalic, sulfuric and succinic acids, taken in equimolecular amounts and under the usual reaction conditions.

4. We studied the reaction mechanism of magnesium alcoholate halides with esters.

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MODELS OF THE MICROSTRUCTURES OF PROTEIN

III. THE STRUCTURE OF PHENYLALANINE ANHYDRIDE DERIVATIVES

L. N. Akimova, I. P. Kuranova and N. I. Gavrilov

In a previous report [1] it was shown that N-aminoacyl derivatives of phenylalanine anhydride were formed especially smoothly and in good yield on treating phenylalanine anhydride with acid chlorides of amino acids. Previously, study of the behavior of N-aminoacyl derivatives of glycine anhydride had shown their exceptional stability in an alkaline medium and particular behavior to hydrazine treatment [2]. This consisted of: 1) the addition of hydrazine at the CO-groups of the phthalyl blocking group when the reaction was carried out in ether or alcohol in the cold, 2) the elimination of the phthalyl group when heated in alcohol and 3) the opening of the diketopiperazine ring to form a phthalyltripeptide hydrazide, without breaking the acyl bond.

In this work we studied the properties of phenylalanine anhydride derivatives and showed how readily they were hydrolyzed by treatment with aqueous and alcohol solutions of alkali and hydrazine. In this way, using the aminoacyl derivatives of two anhydrides (glycine anhydride and phenylalanine anhydride) as examples, we first noticed the effect of the amino acid composition of the anhydride and acyl group on the properties of these derivatives.

The effect of the amino acid composition on the stability of N-aminoacyl and cyclic bonds was noted when investigating the properties of the amino acid anhydride derivatives that we synthesized. It was known, for example, that when treated with 4% NaOH in the cold, glycine anhydride is quantitatively converted to glycylglycine in 20 minutes (Fischer). The aminoacyl derivatives of this anhydride (in which the aminoacyls were phthalylglycyl-, phthalylalanyl-, phthalylvalyl- and phthalylleucyl-) were decomposed to acyltripeptides only after standing for 24 hours under these conditions. In contrast to glycine anhydride, the phenylalanine anhydride that we studied was found to be exceptionally stable. It decomposed (to amino acid) at the $-NH-CO$ bond after heating for 4 hours with 4% NaOH. However, the introduction of amino acid radicals into the molecule of this anhydride made the $-NH-CO$ bond in the ring less stable. Thus, in contrast to phenylalanine anhydride which was decomposed only after prolonged heating, its aminoacyl derivatives were decomposed with 4% NaOH even in the cold. This instability of aminoacyl derivatives of phenylalanine anhydride (in which the aminoacyls were phthalylglycyl-, -alanyl-, -valyl- and -leucyl-) was confirmed by the isolation of phthalyltripeptides from copper biuret complexes and by the capacity of these anhydride derivatives to break down under alkali treatment when titrated in alcohol (by Willstätter's method).

From the given data it follows that the stability of the cyclic bond in aminoacyl anhydrides depends not only on the amino acid composition of the anhydride, but also on the amino acids in the side aminoacyl group. Thus, the stability* of the cyclic bond decreases in the order: N,N'-diphthalylglycyl-, N,N'-diphthalylalanyl-, N,N'-diphthalylvalyl- and N,N'-diphthalylleucyl-phenylalanine anhydrides.

In contrast to the readily decomposed aminoacyl derivatives of phenylalanine anhydride, the same (according to the amino acid composition of the aminoacyls) derivatives of glycine anhydride are exceptionally stable. Thus, the stability of the $-NH-CO$ bond in an isolated ring and in a ring with an N-aminoacyl form of bond was different and depended on the amino acid in the ring and the aminoacyl groups. The stability of the N-acyl and N-aminoacyl bond was, however, directly dependent on the amino acid composition of the anhydride. This was

* According to the rate of formation of copper biuret complexes.

particularly well illustrated by studying the reaction products of anhydride derivatives with hydrazine. Thus, the N-aminoacyl derivatives of glycine anhydride had a more stable bond between the amino acid and diketopiperazine nitrogen than had the derivatives of phenylalanine anhydride. This made it possible for us to use hydrazine to remove the phthalyl blocking group of the N-aminoacyl derivative of glycine anhydride – N,N'-diphthalylglycyl--glycine anhydride. The N-aminoacyl derivatives of phenylalanine anhydride offer a completely different picture. Here the hydrazine effect was limited and consisted of only a specific effect on the N-aminoacyl bond, with the amino acid composition of the acyl group not affecting the specificity of the hydrazine action. Thus, when treated with hydrazine, N,N'-diphthalylglycyl-phenylalanine anhydride, like N,N'-diphthalylalanyl-, phthalylvalyl- and phthalylleucyl-phenylalanine anhydrides, split off aminoacyl groups and not the phthalyl blocking group. In this way, the factor determining the stability of acyl and N-aminoacyl bonds was the amino acid composition of the anhydride.

We had shown previously [3] that, when N-benzyldipeptides were heated in nitrobenzene or glycol, depending on their amino acid composition, they were converted quantitatively to N-benzyldiketopiperazines. We showed the effect of the amino acid composition on the system of conjugated functional groups of amino acids and peptides, using also N-benzyltripeptides [4]. Actually, this effect of amino acids on the properties of N-benzylpeptides was combined with the effect of the benzyl blocking group, which consisted of an increase in the carbonyl functions of the carboxyl. Here, however, the effect of the amino acid composition dominated the effect of the benzyl group. Thus, heating N,N'-dibenzylglycyl-glycyl-glycine gave a diketopiperazine and eliminated N,N'-dibenzylglycine while heating N,N'-dibenzylleucylglycyl-glycine gave N-dibenzylleucine and glycine anhydride. N--benzyltripeptides, which include phenylalanine as the terminal amino acid, formed aminoacyl anhydrides most readily.

Thus, the N-aminoacyl type of bond as one of the chemical bonds of diketopiperazine with amino acids and their derivatives, cannot be studied or examined separately, isolated from the amino acids which participate in its formation.

EXPERIMENTAL

1. N,N'-Diphthalylglycyl-phenylalanine anhydride. 2.27 g (0.0077 mole) of phenylalanine anhydride and 3.44 g (0.016 mole) of phthalylglycine acid chloride were heated in 70 ml of anhydrous xylene. Over 1 hour the bulk of the solid dissolved. Heating was continued for a further 2 hours. The reaction mixture was cooled, the precipitate of unreacted phenylalanine anhydride (0.35 g) filtered off and the xylene filtrate concentrated in vacuum. The crystals, which formed when petroleum ether was added, were filtered off and dried in a vacuum desiccator. The weight was 3.6 g (80%). The m.p. was 243-250°. The substance is not described in the literature. It was readily soluble in chloroform, benzene, xylene and nitrobenzene, but insoluble in water. Under the microscope the crystals from benzene and nitrobenzene appeared as little envelopes. The biuret reaction was positive after the material had stood with alkali. The ninhydrin and picric acid reactions were negative.

Found %: C 68.47; H 4.24; N 8.33. $C_{38}H_{28}O_8N_4$. Calculated %: C 68.25; H 4.18; N 8.36.

To prove the structure we examined the amino acid composition by paper chromatography, the reaction with hydrazine and the biuret reaction.

a) Investigation of amino acid composition. The material was hydrolyzed for 48 hours with 20% hydrochloric acid. Glycine and phenylalanine were found on the paper chromatogram of the hydrolyzate (solvent: butanol–water–acetic acid).

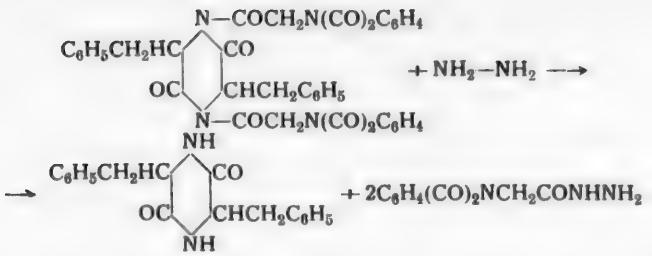
b) Reaction with hydrazine hydrate. 0.1 ml of hydrazine hydrate was added to 0.1 g of N,N'-diphthalylglycyl-phenylalanine anhydride, dissolved in 10 ml of chloroform. After 1 hour, the precipitate was filtered off, washed with absolute ether and dried in a vacuum desiccator. The weight was 0.014 g. The m.p. was 301°.

The precipitate was phenylalanine anhydride. The phthalylglycyl hydrazide, which was isolated by concentrating the chloroform filtrate, was hydrolyzed for 26 hours with 10% HCl. Only glycine was found on the chromatogram (solvent: butanol – water – acetic acid).

Found %: N 23.98. $C_{10}H_9O_3N_3$. Calculated %: N 24.13.

The reaction proceeded quantitatively by scheme 1.

Scheme 1



c) Investigation of copper biuret complex. To 0.5 g of N,N'-diphthalylglycyl-phenylalanine anhydride was added 10 ml of 4% NaOH solution and 4% $CuCl_2$ solution until a permanent precipitate of $Cu(OH)_2$ appeared. The mixture was agitated on a rocker for one day and then filtered through a paper filter to remove the $Cu(OH)_2$ from the solution. The absorption spectrum of the copper complex was plotted. The absorption maximum was at 545 mμ (table). Then the copper complex was decomposed with 10% hydrochloric acid. The precipitate formed was filtered off, washed with water and dried. The weight was 0.19 g. The m.p. 138°.

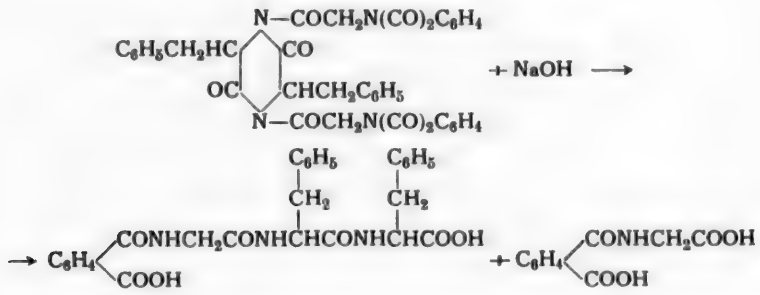
Found %: N 8.37. $C_{28}H_{27}O_7N_3$. Calculated %: N 8.11.

Spectrophotometric Data on the Solutions of the Copper Biuret Complexes

Wavelength λ (in mμ)	Values of optical densities ε		Wavelength λ (in mμ)	Values of optical densities ε	
	N,N'-diphthalylglycyl-phenylalanine anhydride	N,N'-diphthalylalanyl--phenylalanine anhydride		N,N'-diphthalylglycyl--phenylalanine anhydride	N,N'-diphthalylalanyl--phenylalanine anhydride
470	0.258	0.237	560	0.676	0.532
480	0.342	0.300	565	0.652	0.523
490	0.392	0.350	570	0.616	0.490
500	0.428	0.428	575	0.576	0.490
510	0.458	0.462	580	0.558	0.478
520	0.560	0.500	590	0.534	0.440
530	0.658	0.545	600	0.498	0.390
540	0.682	0.543	610	0.432	0.333
545	0.702	0.548	620	0.360	0.290
550	0.700	0.543	630	0.342	0.243
555	0.682	0.530	640	0.282	0.210

Paper chromatographic analysis of the hydrolyzate revealed only two amino acids – glycine and phenylalanine. Thus, the liberation of phthaloylglycyl-phenylalanyl-phenylalanine indicates alkaline decomposition during the biuret reaction proceeding by scheme 2.

Scheme 2



2. N,N'-Diphthalylalanyl-phenylalanine anhydride. a) Phthalylalanyl acid chloride was prepared by the directions for phthalylglycyl acid chloride. From 5 g of phthalylalanine and 5 g of phosphorous pentachloride we obtained 5 g of the acid chloride (90%). The m.p. was 77°.

b) A mixture of 1.3 g (0.0044 mole) of phenylalanine anhydride and 2.12 g (0.0088 mole) of phthalylalanyl acid chloride was heated in 80 ml of anhydrous xylene for 2 hours. The bulk of the solid dissolved. 0.2 g of unreacted phenylalanine anhydride was isolated. The oil remaining after vacuum concentration of the solution was dissolved in the minimum amount of xylene by heating and precipitated with petroleum ether. The precipitate was recrystallized from chloroform. A substance was isolated from the mother liquors on adding petroleum ether. The weight was 1.6 g (62%). The m.p. 197-205°. The material is not described in the literature. It was readily soluble in chloroform, benzene, xylene and nitrobenzene, difficultly soluble in alcohol and insoluble in water. The picric acid and ninhydrin reactions were negative and the biuret reaction positive.

Found %: C 68.94; H 4.91; N 7.94. $C_{40}H_{32}O_8N_4$. Calculated %: C 68.98; H 4.59; N 8.05.

a) Investigation of the amino acid composition revealed alanine and phenylalanine.

b) Reaction with hydrazine. 0.1 ml of hydrazine hydrate was added to a solution of 0.1 g of N,N'-diphthalylalanyl-phenylalanine anhydride in 10 ml of chloroform. The precipitate was filtered off and washed with alcohol. The m.p. of 301° and the properties of the substance isolated indicated that it was phenylalanine anhydride. The phthalylalanyl hydrazide, obtained by concentrating the chloroform filtrate, was hydrolyzed for 26 hours with 10% hydrochloric acid. A paper chromatogram of the hydrolyzate showed only alanine.

Found %: N 17.91. $C_{11}H_{11}O_3N_3$. Calculated %: N 18.02.

Thus, the reaction of N,N'-diphthalylalanyl-phenylalanine anhydride with hydrazine proceeded by scheme 1.

c) The copper biuret complex of N,N'-diphthalylalanyl-phenylalanine anhydride was prepared as described for N,N'-diphthalylglycyl-phenylalanine anhydride. The absorption maximum lay at a wavelength of 545 mμ. Decomposition of the copper biuret complex by acidification with 10% hydrochloric acid yielded 0.15 g of a substance with m.p. 125°. A paper chromatogram of the hydrolyzate (hydrolysis with 10% hydrochloric acid for 24 hours) revealed phenylalanine and alanine.

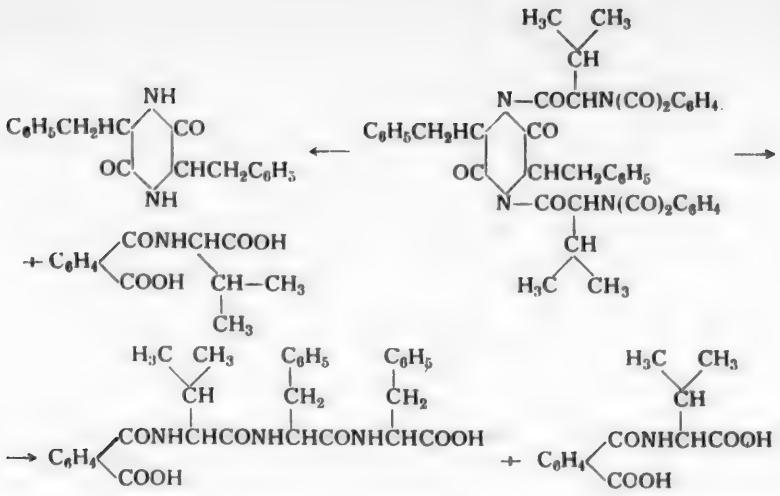
Found %: N 8.15. $C_{29}H_{29}O_7N_3$. Calculated %: N 7.90.

The isolation of phthaloylalanyl-phenylalanyl-phenylalanine on decomposing the copper complex, confirms the decomposition of N,N'-diphthalylalanyl-phenylalanine anhydride under the effect of alkali (under the conditions of the biuret reaction) by scheme 2.

Titration (by the Willstätter method) of phthalylalanylglycine. A 0.1232 g sample was dissolved in 10 ml of 96% ethyl alcohol. It was titrated with 0.1 N alcoholic alkali in the presence of thymolphthalein. The amount of alkali consumed in the titration was 8.96 ml. The theoretical amount of 0.1 N alkali, calculated for phthalylalanylglycine, allowing 2 moles per mole of glycine, was 8.92 ml. Thus, during the titration with alkali the phthalyl group was opened to a phthaloyl one.

Decomposition of N,N'-diphthalylvalyl-phenylalanine anhydride under the effect of 0.1 N alcoholic alkali under titration conditions (by Willstätter's method). A 0.1759 g sample was dissolved in 5 ml of 96% ethyl alcohol. The theoretical amount of alkali for the decomposition of this compound by two moles of alkali (M 752.79) equalled 4.67 ml; the titration required 4.62 ml.

Since further decomposition of this compound by alkali was possible, we added a further 4.62 ml of alkali and left the solution overnight. As a result, all the alkali was consumed and on standing, the solution deposited a precipitate, which was filtered off, washed with alcohol and dried. The m.p. of 291° indicated that the precipitate was phenylalanine anhydride. The weight was 0.01 g, which corresponds to 0.0256 g of N,N'-diphthalylvalyl-phenylalanine anhydride. The theoretical amount of 0.1 N NaOH consumed by the COOH groups liberated in the hydrolysis of this amount of N,N'-diphthalylvalyl-phenylalanine anhydride, allowing 4 moles, was 0.85 ml. As a total of 9.24 ml of 0.1 N NaOH was added, then 8.39 ml was used in neutralization in the decomposition of 0.1503 g of N,N'-diphthalylvalyl-phenylalanine anhydride. On the basis of the titration data, the following scheme is put forward for the decomposition of the latter.



SUMMARY

1. We described the synthesis of N-aminoacyl derivatives of phenylalanine anhydride: N,N'-diphthalylglycyl- and N,N'-diphthalylalanyl-phenylalanine anhydrides.

2. The hypothesis put forward previously on the mechanism of the removal of the N-aminoacyl groups from these compounds by hydrazine treatment was confirmed.

3. Their behavior was studied under the conditions of a biuret protein reaction (4% NaOH) and to show their decomposition under alkali treatment to phthaloylglycyl-phenylalanyl-phenylalanine and phthaloylalanyl--phenylalanyl-phenylalanine.

4. On the basis of titration data (by Willstätter's method) a decomposition scheme for N,N'-diphthalylvalyl--phenylalanine anhydride under alkali treatment is proposed.

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Moscow State University

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*Original Russian pagination. See C. B. Translation.

PREPARATION AND INVESTIGATION OF SOME PROPERTIES OF N-MONOAMINOACYL SUBSTITUTED SARCOSINE DIKETOPIPERAZINES

N. A. Poddubnaia and G. I. Lavrenova

Monoaminoacyl derivatives of amino acids have been studied very little up to now. Monoacyldiketopiperazine was first prepared [1] by reacting diacetyldiketopiperazine with a series of aliphatic and mixed amines in ether and benzene solutions, regardless of the molar ratios of the components.

In this work we synthesized a series of mixed N-monoaminoacyl derivatives of diketopiperazines, containing one tertiary nitrogen atom, in order to study systematically the rules connected with the appearance of such atoms in a molecule. In addition, the introduction of sarcosine into a molecule of the compound being investigated is interesting in itself as this amino acid, together with N-methylvaline and proline, form part of the antibiotic – actinomycin C [2]. The structure of this antibiotic has not yet been proved conclusively but, according to the authors' data, treatment of the compound with hydrazine hydrate gives N-methylvalyl-sarcosine anhydride and leucylproline anhydride, which may be due to rupture of the aminoacyl bond, as was also confirmed in our work.

The sarcosine anhydrides were acylated with the acid chlorides of N-phthalyl substituted amino acids, which were very stable to heating and the diketopiperazines were acylated by them quite well. The N-phthalylaminoacyl derivatives and their properties are given in Table 1.

TABLE 1

Name of compound	Melting point	Yield (in %)
N-Phthalylglycyl-sarcosyl-D,L-valine anhydride	184-185°	63
N-Phthalyl-D,L-valine-sarcosyl-glycine anhydride	187-188°	50
N-Phthalyl-D,L-norleucyl-sarcosyl-D,L-phenylalanine anhydride. .	177	20
N,N'-Diphthalylglycyl-glycyl-D,L-valine.	195	58

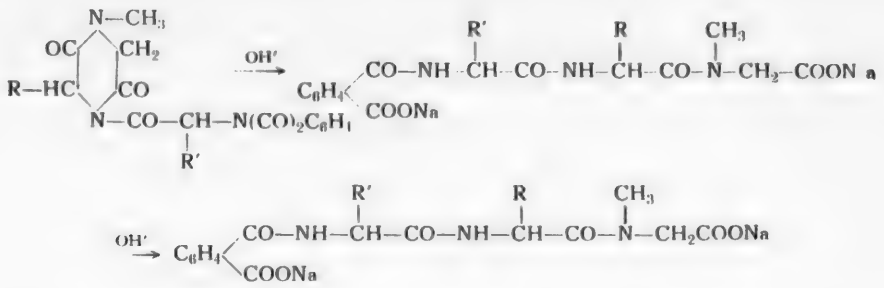
The properties of the compounds obtained were quite similar to those of N,N'-diphthalyl derivatives of glycine diketopiperazines [3-5]. N,N'-Diphthalylglycyl-glycyl-D,L-valine anhydride, whose amino acid composition is similar to that of N-phthalylglycyl-sarcosine-D,L-valine anhydride, had properties characteristic of aminoacyls.

The slow formation of copper complexes* was characteristic of all mono- and diaminoacyl derivatives of diketopiperazines and a displacement of the maximum was observed for both in relation to free tripeptides (Table 2).

As the data in Table 2 show, all monoaminoacyl derivatives of sarcosine anhydrides gave biuret complexes with an absorption maximum close to that of dipeptides, which was apparently due to the presence of a tertiary nitrogen atom as N,N'-diphthalylglycyl-glycyl-D,L-valine anhydride formed a copper complex with an absorption maximum characteristic of tripeptides.

* Due to decomposition of the diketopiperazine ring.

The decomposition of N-phthalylaminoacyl derivatives in an alkaline medium may be shown in the following way.



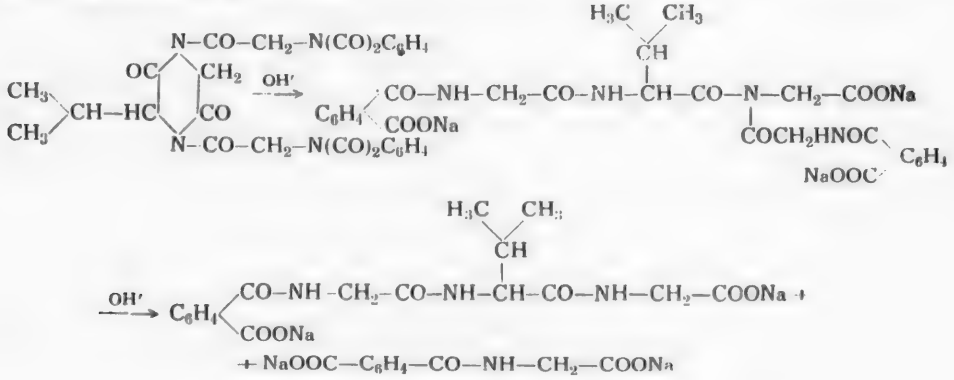
A similar decomposition scheme was proved by synthesizing the aminoacyl derivative of N-phthaloyl-glycyl-D,L-valyl-sarcosine obtained in the decomposition and by identifying it with the compound of similar structure isolated from a solution of the copper complex.

TABLE 2

Name of tripeptide	Absorption maximum λ(mμ)	Name of aminoacyl	Absorption maximum λ(mμ)
Glycyl-D,L-valyl-sarcosine	660 (with excess copper)	N-Phthalylglycyl-sarcosyl--D,L-valine anhydride	640
D,L-Norleucyl-D,L-phenylalanyl-sarcosine	660 (with excess copper)	N-Phthalyl-D,L-norleucyl--sarcosyl-D,L-phenylalanine anhydride	640
D,L-Valyl-glycyl-sarcosine	660 (with excess copper)	N-Phthalyl-D,L-valyl-sarcosyl-glycine anhydride	640
Glycylglycyl-D,L-valine	582	N,N'-Diphthalylglycyl-glycyl--D,L-valine anhydride	560

The phthaloyl group, formed as a result of partial hydrolysis of the phthalyl group, promoted the formation of a biuret complex. After prolonged standing with alkali, the absorption maximum was slowly displaced into the long wavelength region of the spectrum and possibly at the same time the phthaloyl radical was eliminated to form tripeptides, containing sarcosine as the terminal amino acid.

N,N'-Diphthalylglycyl-glycyl-D,L-valine anhydride was decomposed with 2 N NaOH by the following scheme, which was also proved by synthesis.



The acyl group at the tertiary nitrogen atom was unstable and was eliminated in an alkaline medium [4]. The substance synthesized, N-phthaloylglycyl-glycyl-D,L-valine, according to its absorption spectrum and chromatogram, corresponded to the tripeptide isolated after the decomposition of the copper complex. Such a decomposition had been proved previously [6] by determining the amount of free carboxyl groups.

Experiments on the elimination of phthalyl groups by Scheehan and Frank's method [7] did not give positive results as a 1 molar solution of hydrazine hydrate decomposed the compound at the aminoacyl bond to give the original diketopiperazine and amino acid hydrazide. We did observe that the reaction with N-phthalyl-D,L-valyl--sarcosyl-glycine anhydride was considerably more complicated and, probably, formed an aminoacyl derivative; however, the reaction gave such a small yield that it cannot be used as a method for preparing free aminoacyls. Hydrazine hydrate, as shown by numerous examples [8], is a specific reagent for the aminoacyl bond.

EXPERIMENTAL

I. Synthesis of N-Monophthalylaminoacyl Derivatives of Sarcosine Anhydrides

1. N-Phthalyl-D,L-valyl-sarcosyl-glycine anhydride. a) Acid chloride of N-phthalyl-D,L-valine [9]. 2 g (0.008 mole) of phthalyl-D,L-valine was ground in a mortar with 1.7 g (0.008 mole) of phosphorous pentachloride and the mixture heated with 30 ml of absolute benzene on an oil bath at 60°. After the solid had dissolved the solution was heated for a further 1 hour. The benzene was distilled off in vacuum and the oil formed (1.3 g) used for the preparation of the anhydride.

b) N-Phthalyl-D,L-valyl-sarcosyl-glycine anhydride. A mixture of 0.6 g (0.003 mole) of sarcosyl-glycine anhydride and 1.3 g (0.005 mole) of the acid chloride of phthalyl-D,L-valine was heated in 30 ml of absolute xylene at the boiling point of the solvent for 4 hours. After evaporation of the solvent, the crystals were washed with ether to remove phthalyl-D,L-valine and its acid chloride and with water to remove diketopiperazine. The yield was 1.08 g (65%). After a recrystallization from benzene, the melting point was 187-188°. A chromatogram of the hydrolyzate in butanol–water–acetic acid medium (4 : 5 : 1) showed three spots – sarcosine, valine and glycine.

Found %: C 59.88, 59.84; H 5.39, 5.44; N 11.78, 11.73. $C_{18}H_{19}O_5N_3$. Calculated %: C 60.5; H 5.32; N 11.76.

2. N-Phthalyl-glycine-sarcosine-D,L-valine anhydride. The acid chloride of N-phthalylglycine was prepared by the method of Scheehan and Frank [7]. The m.p. was 81-83° (according to literature data: m.p. 83-85°). 2 g (0.009 mole) of the acid chloride of N-phthalylglycine and 1.5 g (0.009 mole of sarcosyl-D,L-valine anhydride was heated under the conditions given above for 5 hours. After evaporation of the solvent, the oil rapidly crystallized on addition of absolute ether and was washed with ether and water. The product was purified by reprecipitation from a saturated benzene solution with absolute ether. The compound obtained was insoluble in water and absolute ether, difficultly soluble in cold benzene and readily soluble in methyl and ethyl alcohols and acetone. The m.p. was 184-185°. A chromatogram of the hydrolyzate showed spots of sarcosine, glycine and valine.

Found %: C60.38, 60.15; H 5.45, 5.60; N 11.87, 11.83. $C_{18}H_{19}O_5N_3$. Calculated %: C 60.30; H 5.38; N 11.82.

3. N-Phthalyl-D,L-norleucyl-sarcosyl-D,L-phenylalanine anhydride. The acid chloride of N-phthalyl-D,L--norleucine was prepared by the method in [10]. The m.p. was 57-58° (according to literature data: m.p. 59°). From 1.6 g of sarcosyl-D,L-phenylalanine anhydride and 2 g of the acid chloride of phthalyl-D,L-norleucine under the given conditions, we obtained 0.66 g (20%) of N-phthalyl-D,L-norleucyl-sarcosyl-phenylalanine anhydride. The m.p. was 177°. A mixed melting point with phenylalanyl-sarcosine anhydride gave a depression of 30°. The anhydride obtained was insoluble in hot and cold water and absolute ether, but was soluble in methyl alcohol and acetone and with difficulty in ethyl alcohol. A chromatogram of the hydrolyzate showed spots of sarcosine, phenylalanine and norleucine.

Found %: C 67.40, 67.22; H 6.06, 6.05; N 9.18, 9.13. $C_{26}H_{27}O_5N_3$. Calculated %: C 67.68; H 5.86; N 9.11.

4. N,N'-Diphthalylglycyl-glycyl-D,L-valine anhydride. 0.5 g (0.003 mole) of glycyl-D,L-valine anhydride and 1.5 g (0.006 mole) of the acid chloride of phthalyl-glycine were ground in a mortar and heated with 20 ml of

absolute xylene at the boiling point of the solvent for 5 hours. After filtration of the solution, the substance was precipitated with absolute ether, the solution evaporated down and carefully washed with water. The product was recrystallized from benzene. The yield was 1.0 g (58%). The m.p. was 195°. The material was soluble in methyl and ethyl alcohols, soluble in benzene on heating and insoluble in ether.

Found %: C 61.21, 61.19; H 4.32, 4.27; N 10.66, 10.68. $C_{27}H_{22}O_6N_4$. Calculated %: C 61.13; H 4.15; N 10.56.

II. Action of 1 Mole of Hydrazine Hydrate in Alcohol on N-Monophthalylaminoacylated sarcosine anhydrides

1. Action of hydrazine hydrate on N-phthalylglycyl-sarcosyl-D,L-valine anhydride. To 0.8 g (0.002 mole) of N-phthalylglycyl-sarcosyl-D,L-valine anhydride was added 2.2 ml of a M solution of hydrazine hydrate in alcohol and 3 ml of ethanol. The mixture was left to stand for 1 hour. We isolated 0.5 g of a substance with m.p. 265°, which reduced copper under the conditions of the biuret reaction. A chromatogram of the hydrolyzate showed one spot – glycine.

According to the analysis data, chromatogram and properties, the substance was phthalylglycyl hydrazide.

Found %: N 20.26, 20.21. $C_{10}H_9O_3N_3$. Calculated %: N 20.17.

The filtrate was concentrated in vacuum and absolute ether added to precipitate 0.21 g of a substance with m.p. 112-114°, which did not depress the melting point of sarcosyl-D,L-valine anhydride. From the melting point and an ascending chromatogram it followed that this compound was sarcosylvaline anhydride (R_f = 0.9).

2. Action of 1 mole of hydrazine hydrate in alcohol on N-phthalyl-D,L-valyl-sarcosyl-glycine anhydride. 1.46 g of N-(phthalyl-D,L-valyl)-sarcosyl-glycine anhydride was heated with 4 ml of a M solution of hydrazine hydrate in alcohol and 12 ml of 96% ethanol. On cooling, the solution deposited 0.03 g of a precipitate, which did not melt at 340° and reduced copper under the conditions of the biuret reaction. A chromatogram of the hydrolyzate, developed with ninhydrin, did not show amino acid spots. The mother liquors yielded a further 0.028 g of the same substance, which was apparently phthalyl hydrazide according to its properties.

Adding water to the alcohol solution gave 0.225 g of a hygroscopic substance, which gave a strong ninhydrin reaction and a blue color in the biuret reaction. It is possible that this substance was D,L-valyl-sarcosyl-glycine anhydride; however an analysis could not be carried out because of the strong hygroscopicity. On a chromatogram in a medium of butanol–water–acetic acid (4 : 5 : 1), there was one spot, different from the starting materials and the decomposition products, which appeared with benzidine and ninhydrin. On an electrochromatogram (ionophoretogram), the D,L-valyl-sarcosyl-glycine anhydride moved 5 cm toward the cathode in an acetic acid buffer over 3 hours with a potential gradient of 6.6 v/cm. A chromatogram of the hydrolyzate gave three spots corresponding to valine, sarcosine and glycine.

III. Absorption Spectra of Copper Complexes of N-Monophthalylaminoacylated Sarcosine Anhydrides

Procedure. 0.01 mole of the substance was dissolved with gentle heating in 9.5 ml of 2 or 4 N NaOH and ¼ M copper acetate solution was added until a large precipitate of copper hydroxide appeared (approximately 0.5 ml). N-Phthalyl-D,L-valyl-sarcosyl-glycine and N-phthalylglycyl-sarcosyl-D,L-valine anhydrides rapidly dissolved in alkali and immediately gave a biuret reaction, whose intensity gradually increased. N-Phthalyl-D,L--norleucyl-sarcosyl-phenylalanine anhydride dissolved with great difficulty in 4 N alkali, even on heating. The intensity of the biuret reaction was very low at first and increased slowly. The results of measuring the absorption spectra maxima are given in Table 3.

In the formation of the copper complex of N,N'-diphthalylglycyl-glycyl-D,L-valine anhydride, a violet color appeared after several minutes and the intensity of this rapidly increased (Table 3).

Isolation of phthaloylglycyl-D,L-valyl-sarcosine from the copper complex. A 0.01 molar solution of biuret copper complex was decomposed by acidification with 10% hydrochloric acid and extracted with benzene, chloroform and ethyl acetate. The extract was dried with calcium chloride and the solvent evaporated to dryness to give a substance which crystallized on standing in a vacuum desiccator. The m.p. was 182°. In the alkaline solution containing copper acetate, a copper complex was formed with an absorption maximum at 640 mμ

(Table 3). The partition coefficient of the substance on an ascending chromatogram with a butanol–water–acetic acid medium, developed with benzidine, corresponded to the N-phthaloylglycyl-D,L-valyl-sarcosine synthesized (R_f = 0.42).

Phthaloylglycyl-D,L-valyl-sarcosine. 1.3 g of the acid chloride of phthalylglycine was dissolved in 10 ml of dioxan and a mixture of 1 g of D,L-valyl-sarcosine and 0.42 g of magnesium oxide in 50 ml of water was added dropwise over a period of 40 minutes with cooling and continuous stirring. The slightly turbid solution was filtered, acidified with hydrochloric acid and evaporated down in vacuum. The needles had m.p. 182°. The substance obtained was soluble in dioxan, chloroform, alcohol and benzene. For purification it was reprecipitated from dioxan with petroleum ether.

Found %: C 54.85, 54.91, H 5.89, 5.90. $C_{18}H_{23}O_7N_3$. Calculated %: C 54.96; H 5.85.

Reaction with copper in an alkaline solution gave a complex with an absorption maximum at 640 mμ, which agreed in the character of the spectrum with that isolated in the decomposition of the copper complex (Table 3).

TABLE 3

Changes in the Absorption Coefficient Maxima of the Decomposition Products of Phthalylaminoacyldiketopiperazines

Name of compound	Change in ε max with time											
	0 hours		2 hours		15 hours		54 hours		78 hours		5 days	
	λmμ	ε	λmμ	ε	λmμ	ε	λmμ	ε	λmμ	ε	λmμ	ε
N-Phthalylglycyl-sarcosyl-D,L-valine anhydride	640	0.370	640	0.612	640	0.620	640	0.642	640	0.650	650	0.650
N-Phthalyl-D,L-valyl-sarcosyl-glycine anhydride	640	0.315	640	0.530	640	0.545	640	0.550	—	—	—	—
N-Phthalyl-D,L-norleucyl-sarcosyl-D,L-phenylalanine anhydride	—	—	—	—	650	0.350	640	0.500	—	—	650	0.512
N,N'-Diphthalylglycyl-glycyl-D,L-valine anhydride	560	0.408	560	0.732	560	0.745	580	0.732	580	0.740	—	—
Phthaloylglycyl-D,L-valyl-sarcosine	—	—	650	0.648	does not change							
Phthaloylglycyl-glycyl-D,L-valine	—	—	560	0.738	does not change							

Isolation of phthaloylglycyl-glycyl-D,L-valine from decomposition of the copper complex of N,N'-diphthalylglycyl-glycyl-D,L-valine anhydride. A 0.01 molar solution of the copper complex was decomposed with 10% hydrochloric acid. The substance was extracted with benzene from the acid solution. The benzene was dried with calcium chloride and evaporated in vacuum. The m.p. of the product was 270°. The substance obtained gave a biuret reaction with an absorption maximum at 560 mμ and on an ascending chromatogram in a butanol–water–acetic acid medium (4 : 5 : 1), developed with benzidine, it corresponded to the tripeptide N-phthaloylglycyl-glycyl-D,L-valine (R_f = 0.62) synthesized.

Phthaloylglycyl-glycyl-valine. 1.1 g of phthalylglycyl-glycine was dissolved in 5 ml of dioxan, cooled and 0.12 ml of triethylamine and 0.1 ml of ethyl chlorocarbonate added. A gelatinous precipitate was formed and after cooling for 10 minutes, it was treated with 0.1 g of valine dissolved in 1.5 ml of dioxan and 0.4 ml of 2 N NaOH. After slight shaking, the reaction mixture became clear. To complete the reaction it was left for 12 hours at room temperature and then concentrated under reduced pressure. The oil formed crystallized in a desiccator. The m.p. was 270°. The product was readily soluble in organic solvents. It was reprecipitated from ethanol with petroleum ether.

Found %: C 53.80, 53.84; H 5.50, 5.55. $C_{17}H_{21}O_7N_3$. Calculated %: C 53.82; H 5.54.

SUMMARY

1. The following N-monophthalylaminoacylated derivatives of sarcosine anhydrides were synthesized for the first time: N-phthalylglycyl-sarcosyl-D,L-valine anhydride, N-phthalyl-D,L-valyl-sarcosyl-glycine anhydride and N-phthalyl-D,L-norleucyl-sarcosyl-D,L-phenylalanine anhydride.

2. The mixed N,N'-diphthalylaminoacyldiketopiperazine – N,N'-diphthalylglycyl-glycyl-D,L-phenylalanine anhydride – was synthesized for the first time.

3. The absorption spectra of the biuret complexes, prepared from N-phthalylaminoacyldiketopiperazines were measured and the scheme for their decomposition in an alkaline medium was confirmed by the synthesis of phthaloylglycyl-valyl-sarcosine and phthaloylglycyl-glycyl-valine.

4. It was shown that cleavage occurred at the aminoacyl bond when N-monophthalylaminoacyldiketopiperazines were treated with hydrazine hydrate.

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INVESTIGATION OF PINACOLIN ISOMERIZATION USING LABELED ATOMS

Z. N. Parnes, S. V. Vitt and D. N. Kursanov

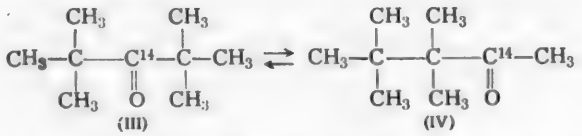
At the present time various investigators have established that aliphatic carbonium ions undergo hydrogen exchange with acids to exchange hydrogen atoms, which are bonded to carbon atoms adjacent to the carbonium center [1-3].

It was also shown [3] that the carbonium center in a carbonium ion, formed by treating a carbonyl compound with sulfuric or another strong mineral acid (at 0°), was incapable of migration, in contrast to the carbonium ion, prepared from a hydrocarbon with a tertiary carbon atom. Thus, on reacting ketones, aldehydes and carboxylic acids with D_2SO_4 or D_3PO_4 only the hydrogen atoms at C_α exchanged.

On the other hand, cases are known of ketone isomerization [4-7] which are explained by the transfer of the carbonium center. Zook and Paviak [6] found that tertiary butyl ethyl ketone (I) when treated with conc. H_2SO_4 for 3 hours at 55° and 2 days at room temperature was 9% converted to tertiary amyl methyl ketone (II).

$$\underset{\text{(I)}}{(CH_3)_3CCOCH_2CH_3} \rightarrow \underset{\text{(II)}}{(CH_3)_3CCH_2COCH_3}$$

Barton and Porter [8] recently proved conclusively that in ketone isomerization the oxygen atom does not transfer from one carbon to another, but that only the hydrocarbon radicals migrate. In order to prove this hypothesis, the authors used ditertiary butyl ketone (III), containing C^{14} in the carbonyl group. It was found that the 2,2,3,3-tetramethylpentanone-4 (IV) obtained by the isomerization contained all the C^{14} in the carbonyl group.

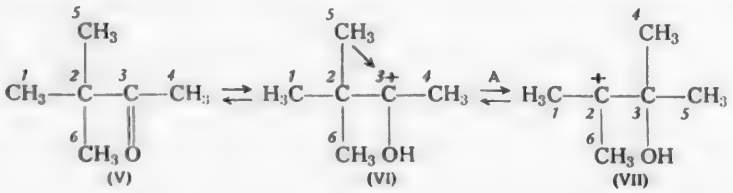


(III) (IV)

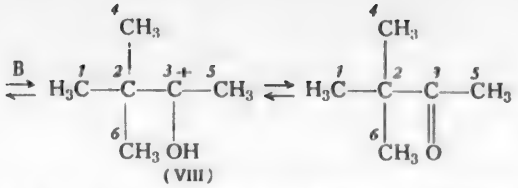
It seemed interesting to us to investigate the reaction of pinacolin (V) with deuterosulfuric acid under the conditions at which the above ketones were isomerized [6].

The assumed isomerization of pinacolin cannot be detected by the usual chemical methods as the reaction product cannot be differentiated from the initial substance; however, one could hope to detect it by using labeled atoms.

According to the data of T. E. Zalesskaia [5] and Barton and Porter, this isomerization should proceed by the following scheme, including the intermediate formation of ion (VII) (asynchronous reaction mechanism).

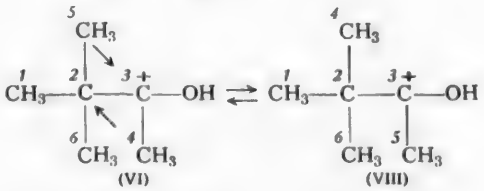


(V) (VI) (VII)



(VIII)

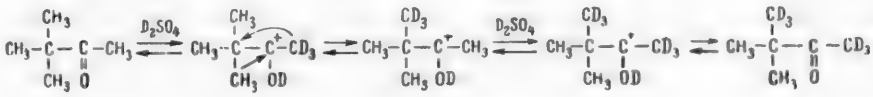
However, on the basis of data we obtained in work on pinacolin rearrangement [9], one can consider that either ion (VII) exists for such a short period that it has no time to enter the hydrogen exchange reaction to any noticeable degree or that it does not form at all and the rearrangement occurs synchronously, i.e., without forming the free ion (VII), as is shown in the scheme below.



(VI) (VIII)

On the contrary, ions (VI) and (VIII) should readily enter the hydrogen exchange reaction. Due to the reversibility of the isomerization, all the hydrogen atoms of pinacolin should be finally exchanged. In this case the trimethylacetic acid, obtained by oxidizing the pinacolin isolated after the reaction, should apparently contain deuterium.

We found that after heating pinacolin with D_2SO_4 at 50° for 10 hours, the tertiary butyl group of pinacolin did not contain deuterium, which indicated the absence of methyl group migration under these conditions. However, after heating at 100° for 11 hours, the pinacolin recovered contained a considerable amount of deuterium in the tertiary butyl group, which corresponded to an exchange of more than three hydrogen atoms. Consequently, under our conditions pinacolin underwent isomerization which, however, due to the similarity of the initial and final substances, cannot be detected readily other than by using labeled atoms.



Synchronous transfer of methyl groups

From the data given above one can assume that hydrogen exchange in this hidden isomerization is the result of the transfer of methyl groups and is not caused by the transfer of the carbonium center.

EXPERIMENTAL

Concentrated D_2SO_4 (19.92 g) (excess density 9050 γ/ml) was gradually added to pinacolin (20.45 g) cooled

Expt. No.	Temp.	Time (in hours)	Excess density of water from combustion (in γ/ml)						
			calculated					experiment	
			semicarbazone			acid		semicarbazone	trimethylacetic acid
			3H	6H	9H	3H	9H		
1	50°	12	7315	—	10030	10970	—	7020	230
2	100	6	7615	9670	—	—	—	10620	—
3	100	11	—	—	—	6675	11760	—	7830

with ice-water. A sealed ampule with the reaction mixture was heated in a thermostat at 100° for 11 hours. At the end of the experiment the reaction mixture was neutralized with Na_2CO_3 or $NaHCO_3$ and extracted with ether. After distillation of the ether, the residue was distilled on a column: b.p. 103-105° (4.7 g). The pinacolin isolated was divided into two parts: a semicarbazone was prepared from the first and the second was oxidized to trimethylacetic acid with NaOBr. The trimethylacetic acid was boiled with a large excess of water, extracted with ether and distilled.

SUMMARY

1. The reaction of pinacolin with deuterosulfuric acid was studied under conditions of ketone isomerization.

It was shown that under these conditions pinacolin exchanged the hydrogen atoms in the tert.-butyl group for deuterium.

2. The reaction mechanism of deuterium exchange and isomerization of pinacolin was examined.

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ALKYLATION OF DIPHENYL WITH ALCOHOLS IN THE PRESENCE OF BF_3 H_3PO_4 CATALYST

I. A. Romadan and S. E. Berga

Aromatic hydrocarbons of natural lubricating oils are homologs of benzene, naphthalene and diphenyl. However, individual substances cannot be separated from the natural mixtures. The only substances that can be investigated are synthetic ones, prepared by various methods. Using the method of Ulmann [1], Schreiner [2] prepared p,p'-diethyl-, p,p'-diisopropyl- and p,p'-ditert.-butyldiphenyls. Boedtker [3] synthesized p,p'-ditert.--amyl- and p,p'-di-n-butyldiphenyls by the same method. p-Monoalkyldiphenyls were synthesized by Japanese chemists [4] by the Friedel-Crafts reaction between diphenyl and acid chlorides, with subsequent reduction of the ketones obtained. They prepared p-n-butyl-, p-n-hexyl-, p-n-octyl- and other alkyldiphenyls. The constants are given in the article.

There are few papers on the alkylation of diphenyl. Thus, Grosse, Mavity and Ipatieff [5] alkylated diphenyl with 2,2,4-trimethylpentane in the presence of $AlCl_3 + H_2O$ and obtained p-tert.-butyldiphenyl; Levine and Cass [6] treated diphenyl with propylene and isopropyl chloride using $AlCl_3$ and obtained mono- and diisopropyldiphenyls; Pokrovskaia and Sushchik [7] reacted hexyl bromide with diphenyl using $AlCl_3$. The well-known paper by Nozakura [8] describes the alkylation of diphenyl in the presence of a Japanese clay catalyst. Here, the practical use of higher monoalkyldiphenyls as oils for diffusion pumps is described. The alkylation of diphenyl with alcohols using the catalyst H_3PO_4 [9] has been investigated and diphenyl has been reacted with various alcohols in the presence of BF_3 [10]. In the last two papers, the authors showed that H_3PO_4 directs radicals into the para-position giving mainly monoalkyldiphenyls in yields of up to 60% (calculated on diphenyl). With BF_3 a mixture of mono- and dialkyldiphenyls was obtained with a considerable predominance of the mono derivative. The total yield of the substances obtained was 74-98%, depending on the starting alcohol.

In the present work we examined the reaction between diphenyl, and isoamyl, isobutyl, isopropyl, n-propyl and n-butyl alcohols in the presence of $BF_3 \cdot H_3PO_4$. It was interesting to determine the directing effect of stronger acid catalysts than BF_3 and at the same time to examine the possibility of isomerizing secondary radicals into tertiary ones in the presence of a strong electrophilic reagent. In previous papers [9, 10] we showed that the alkylation of diphenyl with isobutyl alcohol yielded p-tert.-butyldiphenyl with m.p. 52°. In this work we obtained amyldiphenyl with m.p. 46°. Both substances are analogous to alkyldiphenyls, obtained by alkylating diphenyl with tertiary butyl and amyl alcohols. However, the p-tert.-butyldiphenyl, described in the previous paper [9] was, apparently, not quite pure and was therefore characterized as an oily product. Only after careful distillation on a column could we isolate crystalline substances whose molecular weight and elementary composition corresponded to those of monobutyl- and monoamyldiphenyls. When oxidized with nitric acid in sealed tubes, they gave terephthalic acid. The supposed p-tert.-amyldiphenyl reacted slowly with a bromine solution in carbon tetrachloride.

In the work described we again tried to find confirmation for the hypothesis on the mechanism of alkylation with alcohols in relation to structure. Kenne and Sowa [11] and Price and Lund [12] have expressed opinions on the mechanism of alkylation with alcohols in the presence of BF_3. Later, other authors also tried to explain the mechanism of the reaction [13, 14], but concrete hypotheses on the course of the reaction in relation to the alcohol's structure were not, apparently, put forward. Having examined the alkylation of naphthalene [15, 16] and diphenyl [10] with normal and isoalcohols in the presence of BF_3, we can put forward some hypotheses on the alkylation mechanism based on the following facts. 1) Reactions with normal alcohols gave alkylnaphthalenes and diphenyls with only normal radicals; 2) in alkylation with normal alcohols there are no olefin polymerization products; 3) with

normal alcohols the reaction proceeded 3-4 times more slowly than with isoalcohols; 4) alkylation with isobutyl and isoamyl alcohols gave alkylnaphthalenes—diphenyls, containing tertiary radicals; 5) in the reactions with isoalcohols the product mixture always contained olefin dimers and trimers; 6) with isoalcohols the reaction was complete in 1-2 hours.

From these observations one may presume that condensation occurs with normal alcohols, while alkylation by intermediate olefins occurs with isoalcohols which split off water more readily.

Name of substance	Boiling point		n_D^{20}	d_4^{20}	Melting point	MR	
	at atm. pressure	pressure (in mm)				found	calc.
p-n-Propyldiphenyl	296°	108.4 (0.25)	1.5726	0.9798	1°	193	196
p-p'-Di-n-propyldiphenyl	311	122 (0.2)	1.5570	0.9997	—	—	—
p-n-Butyldiphenyl	299	112 (0.6)	1.5718	0.9684	14	207	210
p-p'-Di-n-butyldiphenyl	317	129 (0.6)	1.5543	0.9622	57	263	266
p-Isopropyldiphenyl	291	103.3(0.34)	1.5692	0.9651	4	200	196
p-Tert.-butyldiphenyl	310	99.3 (01)	—	—	52	208	210
p-p'-Ditert.-butyldiphenyl	326	114.1 (01)	1.5548	0.9502	119	269	266
p-Tert.-amyldiphenyl	300	97 (0.1)	1.5705	0.9671	46	227	224
p-p'-Ditert.-amyldiphenyl	334	124.6 (0.1)	1.5503	0.9479	Little material 114	297	294

The same facts are observed in reactions with $BF_3 \cdot H_3PO_4$ catalysts as in the presence of only BF_3: p-n-alkyldiphenyls were obtained with normal alcohols, p-isopropyldiphenyl — with isopropyl alcohol and p-tert.-butyl- and p-tert.-amyldiphenyls (crystalline substances) formed with isobutyl and isoamyl alcohols. Besides monoalkyldiphenyls, dialkyldiphenyls with radicals in the p,p'-positions were obtained. Their yield did not exceed 8-14%. Polymers of isobutylene and isoamylene were also isolated and investigated. Some characteristics of the alkyldiphenyls are given in the table.

EXPERIMENTAL

The catalyst was prepared by saturating orthophosphoric acid (d 1.86-1.87) with dry BF_3 at room temperature. The molecular compound obtained corresponded approximately to the formula $BF_3 \cdot H_3PO_4$.

The alkylation reaction was carried out in a three-necked flask with a mechanical stirrer and a reflux condenser. The catalyst and the diphenyl were placed in the flask and heated to 160° on an oil bath. Alcohol, which had been previously dried and distilled on a column was added dropwise at this temperature. The end of the dropping funnel dipped into the reaction mixture. After the addition of 3 moles of alcohol, the reaction mixture was heated for from 3 to 12 hours, depending on the structure of the alcohol. The BF_3 liberated during the reaction was absorbed in wash bottles with cooled alcohol (usually the same as that used for the reaction). At the end of the evolution of BF_3, the upper layer was separated and treated with superheated steam to remove unreacted diphenyl and olefins. The oil left in the distillation flask was dried and distilled, first over metallic sodium and then on a vacuum column of 48 theoretical plates.

Alkylation of diphenyl with n-propyl alcohol. 154 g of diphenyl, 187 g of n-propyl alcohol (b.p. 98°, $n^{20}D$ 1.3828, d^{20}_4 0.8034) and 130 g of catalyst was heated at 160-165° for 12 hours. By distillation over metallic sodium we obtained 192 g of a mixture of propyldiphenyls, which were separated on a vacuum column. Monopropyldiphenyl formed about 90% of the total amount of propyldiphenyls. The total yield was 63% (calculated on the starting diphenyl).

Alkylation of diphenyl with isopropyl alcohol. 1 mole of diphenyl and 3 moles of isopropyl alcohol (b.p. 83°, $n^{20}D$ 1.3965, d^{20}_4 0.7883) reacted at 162-165° for 3 hours. p-Isopropyl- and diisopropyldiphenyls were isolated in a total yield of 61%. Propylene polymer with b.p. 100-130° was obtained. It decolorized bromine water and reacted with $KMnO_4$ solution.

Alkylation of diphenyl with n-butyl alcohol. The same ratio of reagents was heated at 165° for 11 hours. Mono- and di-n-butyldiphenyls were obtained in 64% total yield. The mixture of butyldiphenyls had a low solidification point (down to −70°). The p-n-butyldiphenyl, isolated with a vacuum column, had m.p. 14°, which corresponds to the data of Japanese chemists [4], who found m.p. 15.3-16.3° for it. Oxidation of the p-n-butyldiphenyl with an alkaline solution of potassium permanganate (boiling for more than 100 hours) gave p-diphenylcarboxylic acid with m.p. 226° (from alcohol), forming an ethyl ester with m.p. 46° [17]; p,p'-di-n-butyldiphenyl was obtained as an oily substance, from which crystals were isolated with m.p. 57-58° only after the material had stood for 3-4 months. According to Boedtker [3], the m.p. of synthetic p,p'-di-n-butyldiphenyl is 58-59°. The author reported that it was a slowly crystallizing oil and gave the refractive index and the specific gravity. The constants we found were close to those reported by Boedtker.

Alkylation of diphenyl with isobutyl alcohol. 1 mole of diphenyl, 3 moles of isobutyl alcohol (b.p. 108°, $n^{20}D$ 1.3964, d^{20}_4 0.8033) and 0.75 mole of catalyst were heated (160-165°) for 2.5 hours. Distillation on a vacuum column yielded p-tert.-butyldiphenyl with m.p. 52°. A second substance, which had a high boiling point, at first had a solidification point of −17°, but on standing it slowly deposited crystals with m.p. 119° (from alcohol). For p,p'-ditert.-butyldiphenyl, Boedtker reported m.p. 122°. The yield of this substance was 6-8%. It did not react noticeably with bromine at room temperature. The molecular weight and elementary analysis of a third substance corresponded to a monobutyldiphenyl; however it was oily, had a solidification point of −9° and the refractive index and specific gravity were different from those of p-tert.-butyldiphenyl.

Alkylation of diphenyl with isoamyl alcohol. 154 g of diphenyl, 264 g of isoamyl alcohol, carefully distilled on a column, and 130 g of catalyst were heated (160-165°) for 3 hours. We obtained p-tert.-amyldiphenyl (m.p. 46° from anhydrous alcohol). A substance slowly (after standing for 2 months) crystallized from the oily product and had b.p. 310°.

Found %: C 90.02; H 9.93. $C_{20}H_{26}$. Calculated %: C 90.16; H 9.84.

A second substance with b.p. 334° slowly crystallized from methyl alcohol after standing for a month and had m.p. 114°; it reacted with bromine dissolved in CCl_4; the molecular weight and elementary composition corresponded to diamyldiphenyl. Apparently this was p,p'-ditert.-amyldiphenyl, which Boedtker [3] synthesized by Ulmann's method [1]. For it the author reported b.p. 224° (16 mm), $n^{16}D$ 1.5503. We found $n^{20}D$ 1.5503. The yield was 4%.

Found %: C 89.66; H 10.38. $C_{22}H_{30}$. Calculated %: C 89.73; H 10.27.

SUMMARY

1. It was suggested that condensation occurs when diphenyl is heated with normal alcohols and therefore only substances with normal radicals are obtained.

2. With isoalcohols the main reaction is that of alkylation with intermediate olefins and therefore alkylnaphthalenes and alkyldiphenyls containing tertiary radicals are obtained.

3. Alkylation of diphenyl with alcohols in the presence of $BF_3 \cdot H_3PO_4$ required 3 moles of alcohol per mole of hydrocarbon, while alkylation with molecular compounds of alcohols and BF_3 needed only 1.5 moles.

4. The alkyldiphenyl yields were 80-98% in the alkylation of diphenyl with molecular compounds. Reaction with a mixed catalyst however, gave a yield of not more than 65%, although the heating time was increased almost two-fold.

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**In Russian.

CASES OF HINDERED POLYMERIZATION OF MONOMERS IN THE ARYL METHACRYLATE SERIES

M. M. Koton, T. A. Sokolova, M. H. Savitskaia and T. M. Kiseleva

In studies of the polymerization of aryl methacrylates it has been discovered that some of these, having substituents in the benzene nucleus ortho to the acyl radical, polymerize considerably more slowly than the corresponding para isomers. In order to clarify the problem of the causes of the hindered polymerization of ortho-substituted aryl methacrylates, various such ortho- and para-substituted derivatives were synthesized. If, in these cases, the polymerization process depends on the nature of the substituent, then for example, o- and p-methoxyphenyl methacrylates would polymerize differently from o- and p-nitrophenyl methacrylates because the nitro and methoxy groups are opposite in character. However, it has been shown that in spite of the difference in the nature of the substituents, in both cases the para derivatives polymerize readily and the ortho derivatives with considerably more difficulty (see table). Consequently it is evident that it is the position of the substituent, and not its chemical nature, that determines the behavior of the monomers being compared.

In addition to the methacrylate monomers mentioned above, o- and p-tolyl- and o- and p-diphenyl methacrylates were also synthesized. For the ortho- and para-tolyl methacrylate isomers a quantitative examination of their polymerization was carried out by determination of the percentage conversion by precipitation of the polymer. It was shown that o-tolyl methacrylate did not polymerize at all on heating for 2.5 hours at 80° with 0.3% (by weight) of benzoyl peroxide, whereas the para isomer under identical conditions gave 11.8% conversion. Similarly, a very marked difference was shown also by the diphenylmethacrylate ortho and para isomers.

The proximity of the substituents in the ortho derivatives impedes their polymerization and this can evidently be explained by steric hindrance. The effect on polymerizability of substituting the phenyl by the cyclohexyl radical in the methacrylate molecule was shown by the example of thymol and menthol derivatives.

The methacrylate ester of thymol, containing the bulky isopropyl group, polymerizes with difficulty. Evidently steric hindrance is here connected with the coplanar configuration of the benzene ring, which imparts a definite rigidity to the molecule. The methacrylate ester of menthol analogous to this (but having a hydrogenated nucleus in the molecule) polymerizes readily under ordinary conditions. This can be explained by the fact that the carbon atoms in the cyclohexyl ring do not lie in the same plane; consequently the whole molecule of this compound is not rigid like the methacrylate ester of thymol.

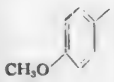
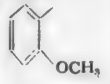
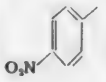
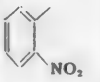
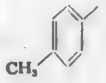
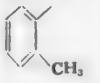
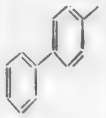
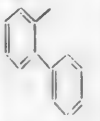
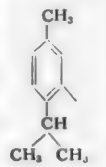
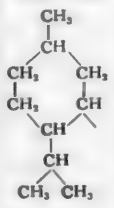
In all these cases hindering of polymerization by a free-radical mechanism can possibly be explained by the screening action of groups that are bulky in relation to the double bond. These groups hinder the addition to the double bond of benzoyl peroxide free radicals, which are also of rather large bulk.

The monomers used in the present investigation were synthesized by methods described in the literature. Their properties are described in the experimental part, where literature data for the compounds described are also quoted for comparison. The p-tolyl, o- and p-methoxy phenyl and o-diphenyl methacrylates as well as the methacrylate esters of thymol and menthol were synthesized for the first time.

EXPERIMENTAL

Preparation of o-methoxyphenyl methacrylate. 37.2 g of guaiacol was dissolved in 200 ml of 5% aqueous sodium hydroxide. 31.5 g of methacrylyl chloride was added from a dropping funnel, with stirring, over a period of 0.5 hours. Stirring was continued for 1 hour at room temperature. The liquid product was then extracted with

Polymerizability of Monomers of the General Structure $CH_2=C(CH_3)-COOR$

No.	Monomer	R	Conditions and results of polymerization
1	p-Methoxyphenyl methacrylate		Polymerizes on heating in the presence of 0.3% (by weight) of benzoyl peroxide.
2	o-Methoxyphenyl methacrylate		Does not polymerize with 0.3% benzoyl peroxide. Becomes viscous on further heating for 120 hours at 120°. with 0.5% benzoyl peroxide.
3	p-Nitrophenyl methacrylate		Polymerizes on heating with 0.3% benzoyl peroxide.
4	o-Nitrophenyl methacrylate		Does not polymerize on heating with 0.3% benzoyl peroxide. Polymerizes only with 2% benzoyl peroxide.
5	p-Tolyl methacrylate		Forms 7% of polymer on heating for 2 hours at 80° with 0.3% benzoyl peroxide and 11.8% polymer after 2.5 hours.
6	o-Tolylmethacrylate		Does not polymerize after 2.5 hours heating with 0.3% benzoyl peroxide.
7	p-Diphenyl methacrylate		Polymerizes on heating in the presence of 0.3% benzoyl peroxide.
8	o-Diphenyl methacrylate		Polymerizes with 0.3% benzoyl peroxide only on prolonged heating (about 200 hours) at 120°.
9	Methacrylic ester of thymol		Does not polymerize with 0.3% benzoyl peroxide. Becomes viscous on further heating with 0.5% benzoyl peroxide for a period of 120 hours at 120°.
10	Methacrylic ester of menthol.		Polymerizes with 0.3% benzoyl peroxide under normal conditions.

ether. The extract was washed with alkali solution and water to neutral reaction, dried over anhydrous magnesium sulfate, the ether distilled off, and the residue twice fractionated in vacuo. The o- and p-tolyl and o- and p-diphenyl methacrylates as well as the methacrylate ester of thymol were prepared by the same method.

Preparation of the methacrylate ester of menthol. 15.6 g of menthol was placed in a round-bottomed flask fitted with a mechanical stirrer and reflux condenser; the menthol was melted, and 12 g of methacrylyl chloride was added with stirring and heating to 80°; after the addition, heating at 80° was continued for 3 hours. The liquid product was extracted with ether. The extract was washed with a 5% solution of sodium hydroxide, and subsequently with water, to neutral reaction. The ether was distilled from the extract after drying over anhydrous magnesium sulfate and the residue fractionated in vacuo. p-Methoxy phenyl methacrylate was prepared in the same way.

Preparation of o-nitrophenyl methacrylate. A mixture of 1 mole of o-nitrophenol and 2 moles of methacrylyl chloride was heated for 2 hours in pyridine, in a flask with a reflux condenser, at the boiling point of the mixture. The mass, solidified by cooling, was washed with water to remove pyridine and the residual oil, after washing with sodium hydroxide solution and water, and drying, was distilled in vacuo.

p-Nitrophenyl methacrylate was prepared in the same way.

Properties of the Monomers

o-Methoxyphenyl methacrylate is a colorless oil, which redistils at 109-110° at 4 mm. Yield 51%, $n^{25}D$ 1.5235.

Found %: C 68.67; H 6.53. $C_{11}H_{12}O_3$. Calculated %: C 68.75; H 6.25.

p-Methoxyphenyl methacrylate crystallizes in the form of colorless plates, m.p. 63-64°. Yield 53%.

Found %: C 68.58; H 6.25. $C_{11}H_{12}O_3$. Calculated %: C 68.75; H 6.25.

p-Tolyl methacrylate. Colorless liquid, b.p. 103° at 7 mm. Yield 72%, d^{20}_4 1.025, $n^{20}D$ 1.5135.

o-Diphenyl methacrylate. Colorless liquid, b.p. 144-145° at 4 mm. Yield 50%, d^{20}_4 1.107, $n^{20}D$ 1.5897.

Found %: C 80.56; H 6.17. $C_{16}H_{14}O_2$. Calculated %: C 80.67; H 5.88.

Methacrylic ester of thymol. Colorless liquid with an aromatic odor. B.p. 127° at 10 mm. Yield 53%, $n^{22}D$ 1.5070.

Found %: C 77.13; H 8.33. $C_{14}H_{18}O_2$. Calculated %: C 77.06; H 8.25.

Methacrylic ester of menthol. Colorless liquid, b.p. 107-108° at 6 mm. Yield 68.1%, $n^{17}D$ 1.4025.

Found %: C 75.11; H 10.95. $C_{14}H_{24}O_2$. Calculated %: C 75.0; H 10.71.

o-Tolyl methacrylate. Colorless liquid, b.p. 99° at 7 mm. Yield 67.6%, d^{20}_4 1.034, $n^{18}D$ 1.5112, (according to literature data [1] b.p. 98-103° at 5 mm, d^{20}_4 1.031, $n^{18}D$ 1.5160).

p-Diphenyl methacrylate. Colorless crystals, m.p. 111-112° (according to the data of [1], m.p. 110°).

o-Nitrophenyl methacrylate. Oily, yellow liquid, b.p. 138-139° at 5 mm. Yield 46.1% (according to the data of [2], b.p. 134-136° at 2 mm).

p-Nitrophenyl methacrylate. Colorless needles, m.p. 95° (according to the data of [2], m.p. 93-94°). Yield 60%.

Polymerization of the Monomers

Polymerization of the methacrylates under investigation was carried out in bulk, under identical conditions. Where there were any variations these are indicated in the table. A weighed sample of about 2 g of monomer was placed in a glass ampoule, to which was added 0.3% (by weight) of initiator (benzoyl peroxide). The ampoule, cooled in solid carbon dioxide, was sealed in an atmosphere of air. Heating of the ampoule was carried out in a thermostat. Starting at 70° the temperature was raised every 24 hours to 80, 100 and 120°. Exception was made for those monomers with melting points above 70°. In these cases, heating was commenced a few degrees above the melting point in order to ensure homogeneity of the medium. The end point of polymerization was decided by the deposition of polymer on the glass.

SUMMARY

1. It has been shown that ortho-substituted aryl methacrylates display hindered polymerization in comparison with their para isomers.

2. This hindered polymerization can be explained by steric hindrance in the monomer molecule.

3. The polymerizability of ortho-substituted methacrylates increases markedly in changing from the coplanar aromatic radical to the corresponding, noncoplanar cycloparaffin radical.

4. The methacrylate esters of p-cresol, guaiacol, p-methoxyphenol, o-hydroxydiphenyl, thymol and menthol, not previously described in the literature, have been synthesized and characterized.

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THE STRUCTURE OF THE POTASSIUM-DIVINYL (BUTADIENE) POLYMER

A. I. Iakubchik and N. N. Motovilova

The dependence of the properties of the polymer and its content of external double bonds* on the nature of the alkali metal used as polymerization initiator, and on reaction temperature, has been established by a number of investigators [1]. In the present work it was proposed to examine the effect of the degree of polymerization on the content of 1,2 linkages in the polymers and on some of their properties (glass temperature, coefficient of freeze-resistance). The polymer obtained by the polymerization of gaseous butadiene by the action of potassium, was chosen as the material to be investigated for the solution of this problem. This polymer is different in many respects from SKB rubber, produced by the polymerization of butadiene in the presence of sodium.

Ozonolysis, first used by Harries in the study of the structure of various rubbers [2], was chosen as the method of investigation, and also a method based on the different rates of oxidation of the internal and external double bonds in the polymer, by benzoyl hydroperoxide (perbenzoic acid) [3-6]. The determination of the polymer structure by the ozonolysis method depended on a single, specific, structural characteristic, namely on the content of 1,2 linkages, that form formic acid and formaldehyde in the final stage of ozonolysis. For the determination of formic acid the method of Fincke [7], based on the reduction of mercuric to mercurous chloride, was used; for the determination of formaldehyde the method of Fosse [8], based on the formation of the condensation product of formaldehyde with β-naphthol, has been acknowledged to be the most suitable, giving more reproducible results than other methods proposed for this purpose.

TABLE 1

No. of sample	Increment of polymer (g. per 1 g. metal)	Proportion of 1,2 segments (%)	Glass temp.	Coefficient of freeze-resistance of vulcanizate
1	160	62.0	—	0.30
2	255	60.0	—60.5°	0.36
3	—	64.8	—59.0	0.27
4	515	58.4	—61.0	0.43
5	765	57.2	—62.0	0.43
6	1000	59.0	—61.0	0.30
7	1520	55.8	—62.0	0.43
8	2000	54.0	—63.5	0.48

* The grouping $-CH(-CH=CH_2)-CH_2-$, formed by combination of butadiene molecules in the 1,2 position, are called segments with external double bonds; segments with internal double bonds $-CH_2-CH=CH-CH_2-$ are formed by combination in the 1, 4 position.

For the determination of total unsaturation, which is necessary for the quantitative determination of 1,2 and 1,4 segments in the polymer, use was made of the reaction with iodine monobromide which, as A. A. Vasil'ev [9] has shown, gives more reliable results than the reaction with iodine monochloride, normally used. In order to be able to calculate the percentage of the carbon skeleton occurring in 1,2 polymer segments, elementary analysis of the polymer samples was carried out, which also allows the extent of oxidizability of the polymer (purified) to be determined. Polymers obtained at different degrees of polymerization, measured by the so-called "increment," i.e., the quantity of polymer per 1 g of metal, were investigated. The results obtained are given in Table 1.

The data presented indicate a tendency to some degree of lowering of the content of 1,2 segments, which is confirmed by a parallel lowering in the glass temperature of the polymer and an increase in the coefficient of freeze-resistance of its vulcanizate. The reduction in the content of segments with external double bonds could be explained by isomerization of such segments during the polymerization process or during ozonolysis, which has been established by a number of investigators [10-12]. Another explanation might be an increase in the actual polymerization temperature resulting from deterioration of the heat-removal conditions with increasing "increment" of polymer; the latter explanation is the most probable and is confirmed by the small increase in content of 1,4 segments found in the polymer.

EXPERIMENTAL

The initial polymer was obtained by passing gaseous butadiene at 10° (in a bath) over a 5% dispersion of potassium in paraffin, placed in flasks on a framework. Polymerization was carried out simultaneously in eight flasks and was interrupted after the attainment of a chosen "increment," determined by weighing. Thus 8 samples of polymer were obtained with increments varying between 150 and 2000. In order to prevent the possibility of oxidation the samples were treated with 2% Neozon D. Purification of the polymer was carried out by reprecipitation by alcohol from benzene solution with subsequent drying to constant weight at 30°, in vacuo. The samples were stored in sealed tubes, filled with purified nitrogen.

Ozonolysis was carried out in ~1% chloroform solution with a constant ozone concentration in the gas (3-4%) obtained by maintaining a constant gas flow (20 liters per hour) and keeping a constant voltage on the transformer winding of 95-100 v. The method of ozonolysis was the same as that described earlier [13]. After completion of ozonolysis the chloroform was distilled off in vacuo, the ozonide dissolved in ether and kept in ether for a period of 15-20 hours. After the ether was distilled off, the ozonide was dried to constant weight and decomposed by heating with a 10-fold quantity of water. The resulting aqueous solution was transferred to a measuring flask from which test portions were removed for determination of formaldehyde. Results of these determinations are given in Table 2.

TABLE 2

No. of sample	Weight of precipitate Hg_2Cl_2 (in g)	Weight of formic acid in ozonide decomposition products	Carbon content of formic acid obtained (in g)	Weight (in g)		
				Dihydroxydinaphthylmethane precipitate*	Formaldehyde in ozonide dec'mp products	Carbon content of formaldehyde obtained
1	0.7461	0.7265	0.1889	0.00181	0.181	0.0724
2	0.8026	0.7826	0.2035	0.00110	0.110	0.0440
3	0.7148	0.6964	0.1931	0.00176	0.176	0.0704
4	0.6890	0.6718	0.1746	0.00134	0.134	0.0536
5	0.6152	0.5998	0.1559	0.00108	0.108	0.0432
6	0.5597	0.5457	0.1419	0.00154	0.154	0.0616
	0.6961	0.6787	0.1765	0.00109	0.109	0.0436
7	0.6953	0.6779	0.1762	0.00118	0.118	0.0472
	0.6906	0.6729	0.1750	0.00093	0.093	0.0376
8	0.5679	0.5437	0.1414	0.00091	0.091	0.0364

* After recalculation to 10 g of solution of ozonolysis products.

Determination of the content of 1,2 segments on the basis of the data obtained was carried out by the method described in an earlier paper [13]. The data obtained are given in Table 3.

TABLE 3

No. of sample	Results of elementary analysis** (in %)		Weight of carbon		% carbon skeleton found in formic acid and formaldehyde	Content of 1,2 segments in the rubber (%)
	C	H	In formic acid and formaldehyde	In sample taken for ozonolysis		
1	87.91	11.66	0.2613	1.68	15.5	62.0
2	88.58	11.45	0.2475	1.65	15.0	60.0
3***	88.34	11.46	0.2515	1.55	16.2	64.8
4	87.45	11.22	0.2282	1.56	14.6	58.4
5	88.61	11.30	0.1831	1.28	14.3	57.2
6	88.12	11.57	0.1854	1.29	14.75	59.0
			0.2380	1.56		
7	88.11	11.53	0.2234	1.56	13.95	55.8
			0.2122	1.56		
8	87.80	11.31	0.1758	1.31	13.5	54.0

* Mean of two determinations. Calculated for butadiene polymer: C 88.88; H 11.11.

** Increment figure unknown.

In using the method of oxdiation of the polymer with benzoyl hydroperoxide (perbenzoic acid) it was intended only to obtain the oxidation curves and compare them with the oxidation curves of the dimer of butadiene (vinyl--1-cyclohexene-3), with the object of clarifying the question of whether any change in the amount of internal double bonds, which serves as a measure of the initial combination of butadiene molecules in the 1,4 position, takes place during the polymerization process. Oxidation of the internal double bonds in the polymer was considered to be complete when in a parallel experiment on the oxidation of the dimer the reaction reached 50%, which corresponds to oxidation of all the internal double bonds. Although the method in this form cannot be considered sufficiently accurate, nevertheless it is possible to decide approximately that the proportion of 1,4 segments is about 40%, there being some increase depending on the depth of polymerization. Thus,for example, for samples 1,4 and 7, with the same degree of oxidation of the dimer (51%), the following figures were obtained for the content of 1,4 segments: 41.8, 42.2 and 44.8%. On determination of the total unsaturation by reaction with iodine monobromide, values were obtained (for purified polymer) fluctuating between the limits 90.0 and 91.9%, no systematic variation with depth of polymerization being observed.

SUMMARY

1. The content of segments with external double bonds in potassium-butadiene polymer, determined by the ozonolysis method, decreases to some extent with increasing depth of polymerization. The values of the glass temperature of the polymer and of the coefficient of freeze resistance of the vulcanizate change correspondingly.

2. The number of segments with internal double bonds, determined by oxidation with benzoyl hydroperoxide (perbenzoic acid), remains practically constant; the data obtained are not sufficiently accurate to draw rigid quantitative conclusions.

3. The unsaturation of the polymer, determined by reaction with iodine monobromide, remains constant.

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INVESTIGATIONS ON CONJUGATED SYSTEMS

LXXXIII. THE STRUCTURE AND REACTIVITY OF THE METHYL ESTER OF VINYLACETYLENE CARBOXYLIC ACID

A. A. Petrov, K. B. Rall and G. I. Semenov

In connection with the systematic investigations that we had undertaken on addition reactions of compounds with double and triple bonds, we were interested in the reactivity of vinylacetylene carboxylic acid and its derivatives. Vinylacetylene carboxylic acid was synthesized as far back as 1938, but the pure acid had not been isolated in the pure form. At the same time its esters were found to possess adequate stability; they have been isolated in the pure form and characterized [1]. Addition reactions of vinylacetylene carboxylic acid and its esters have not been studied.

We prepared the methyl ester of vinylacetylene carboxylic acid by the previously described method and investigated its reaction with bromine. The experiments showed that addition of bromine is very slow and is accelerated by light (Fig. 1). The resultant dibromide changes appreciably when distilled in vacuo (5 mm); we therefore decided to determine its structure with the help of the infrared spectrum without isolating it from the solution in CCl_4 in which the bromination was effected. It was earlier shown that the infrared spectra of dibromides of vinylacetylenic compounds enable precise determination of their structure [2, 3].

The infrared spectrum of the original methyl ester of vinylacetylene carboxylic acid was plotted in advance. This was necessary for evaluation of the structure of the dibromide and there were no data in the literature.

For the purpose of comparison, the spectra of the methyl ester of propiolic acid and of the dimethyl ester of acetylene dicarboxylic acid were plotted under the same conditions. The literature contains details of the vibrational spectra of these esters [4, 5].

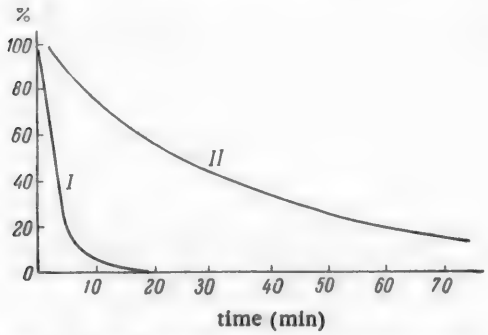


Fig. 1. Rate of bromination of vinylacetylene carboxylic ester in the dark (II) and in diffused light (I).

In the range of frequencies corresponding to the valence CH vibrations the infrared spectrum of the methyl ester of vinylacetylene carboxylic acid contains six bands. Three of these belong to the methyl radical, possibly with superposition of other frequencies (2976, 2907 and 2849 cm^{-1}). These bands are also present in the spectra of the methyl esters of propiolic and acetylene dicarboxylic acids, as well as in the spectra of methanol and dimethyl ether[6]. The other two bands are characteristic of compounds containing the vinyl group (3135 and 3049 cm^{-1}) [7]. Both of these frequencies are also present, however, in the spectra of the methyl esters of propiolic and acetylene dicarboxylic acids which of course do not contain vinyl groups. The frequency of about 3400 cm^{-1} is developed in the spectra of acetylenic aldehydes and ketones and is absent from the spectra of vinylacetylenic hydrocarbons [7, 8]. We assume that this is an overtone (1700 × 2).

The ester of propiolic acid absorbs strongly at 3280 cm^{-1} (ν_{CH} of the terminal acetylenic group).

In the region of frequencies of the deformation CH vibrations the spectrum of vinylacetylene carboxylic acid contains two frequencies (1447 and 1272 cm^{-1}). A frequency of 1414 cm^{-1} is characteristic of the vinyl group. Here this frequency is not differentiated. The 1272 cm^{-1} frequency is very strong, probably due to superposition of several frequencies.

The nonplanar CH vibrations are represented by a pair of frequencies characteristic of the vinyl group (945 and 973 cm^{-1}). The lower frequency has a value slightly higher than in the spectra of hydrocarbons. Acetylene dicarboxylic acid ester does not absorb in this region. Propiolic ester has an intense band at 992 cm^{-1} which is also represented in the spectra of α,β-unsaturated acetylenic aldehydes and ketones. This is probably caused by the CC vibrations at the bond between the carbonyl and the acetylenic grouping.

The strong 2247 cm^{-1} band corresponds to the triple bond. Vinylacetylenic hydrocarbons are characterized by a higher frequency [7] and acetylenic aldehydes and ketones [8, 9] as well as the nearest homolog of vinylacetylene carboxylic ester [5] by a lower frequency of the triple bond. The acetylenic bond also corresponds to a higher value of $\nu_{C\equiv C}$ in the spectrum of propiolic acid ester than in the spectra of acetylenic aldehydes and ketones. No absorption occurs in the spectrum of acetylene dicarboxylic acid ester due to the symmetry of the molecule in the region where the bands characteristic of disubstituted acetylenes are usually observed.

In the spectrum of the methyl ester of vinylacetylene carboxylic acid the double bond is represented by the strong 1608 cm^{-1} frequency. The same frequency was found in the spectra of vinylalkylacetylenes [7].

All of the three esters that were compared have an extremely intense $\nu_{C=O}$ absorption band at 1730 cm^{-1}. According to the literature propiolic and acetylene dicarboxylic acid esters absorb at 1720 cm^{-1} [5].

The ester grouping is evidently associated in all of the spectra with bands in the 1120-1200 cm^{-1} region.

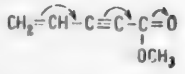
All of the spectra are rich in frequencies of low and medium intensity (probably overtones and proper frequencies).

The spectrum of the dibromide of vinylacetylene carboxylic ester differs from the spectrum of the original ester in being free of appreciable absorption in the 1600 cm^{-1} region and in containing only one band in the 900--1000 cm^{-1} region. Consequently the dibromide no longer contains the vinyl group.

No appreciable increase of absorption occurred in the 1950 cm^{-1} region, which is evidence of the absence of appreciable quantities of the allenic dibromide from the solution.

At the same time the absorption band of the acetylenic grouping was, as before, extremely stong. It has therefore been established that the dibromide of the methyl ester of vinylacetylene carboxylic acid is an acetylenic compound. Consequently addition of bromine took place at the double bond, i.e., in the same manner as in vinylacetylenic hydrocarbons of analogous structure – vinylalkylacetylenes [10].

In the molecule of vinylacetylene carboxylic acid ester, the shift of electrons in the direction of the carbonyl group strongly reduces the reactivity of the double and triple bonds. The double bond, however, turns out to be more reactive to bromine, and the attack evidently does not start at the terminal carbon atom.



A certain relation was previously established between the band intensities of double bonds in the infrared spectra and the reactivity of a system of these bonds [7]. The infrared spectrum of vinylacetylene carboxylic ester is similar to the spectra of those hydrocarbons that add on bromine at the double bond.

EXPERIMENTAL

Vinylacetylene carboxylic acid was prepared by the action of carbon dioxide on vinylacetylene magnesium bromide. Its methyl ester was prepared by the procedure of I. N. Nazarov and M. V. Kuvarzina [1]. The two other esters were prepared from the corresponding acids and methyl alcohol under the action of sulfuric acid in the cold. The constants of all of the esters agreed with the literature data.

Principal Absorption Bands in the Infrared Spectra

Methyl ester of propiolic acid	Methyl ester of vinylacetylene carboxylic acid	Methyl ester of acetylene dicarboxylic acid	Dibromide I	Methyl ester of propiolic acid	Methyl ester of vinylacetylene carboxylic acid	Methyl ester of acetylene dicarboxylic acid	Dibromide (I)
3401 m	3401 m	3401 m	3378 w	**1730** vs	**1730** vs	**1730** vs	**1730** vs
3279 s	—	—	—	—	**1608** s	1634+ s	—
3106 m	3135+ m	3175+ m	—	1560+ m	—	—	—
3049 s	3049 s	3030 s	3003 m	1522+ m	1508+ m	1499+ s	—
3021 s	—	—	—	1441 s	1447 s	1441 s	1441 s
2976 s	2976 s	2976 s	2941 s	—	—	—	1377 m
2907+ m	2907+ s	2899+ m	—	—	—	—	1326 s
2825 m	2849+ s	2833 m	2817 m	1263 s	1272 vs	1269 vs	1280 s
2710 w	—	2762+ w	—	1232+ s	1199 s	—	1172—1248 s
2646 w	2660 w	2618 w	—	1131 s	1124 s	1126+ s	1121 s
2571 w	—	2551 w	—	1080 m	—	—	—
—	2513 w	2494 w	2494 vw	1040 m	1046 s	1046 s	1038 s
2427 m	2457 vw	2375 w	2392 vw	992 s	—	—	—
2320 w	2364+ w	2326 w	—	—	**976** vs	—	—
2304 w	2304+ m	—	—	—	**945** vs	—	954 m
—	**2247** vs	—	**2260** s	858 s	—	895 s	885 m
2137 s	2151+ w	2160 m	2146 vw	—	804 s	826 s	—
—	—	2114 m	—	765 s	776+ m	761 s	—
—	2062 m	2012 m	2062 m	723—707 m	749 s	—	—
1980 m	1961 m	1942 w	1965 w	—	695 m	—	694 w
—	1908 m	1980+ m	—				

Note. The plus sign denotes frequencies appearing as superpositions on other, more differentiated frequencies. s = strong, m = medium, vs = very strong, w = weak, vw = very weak.

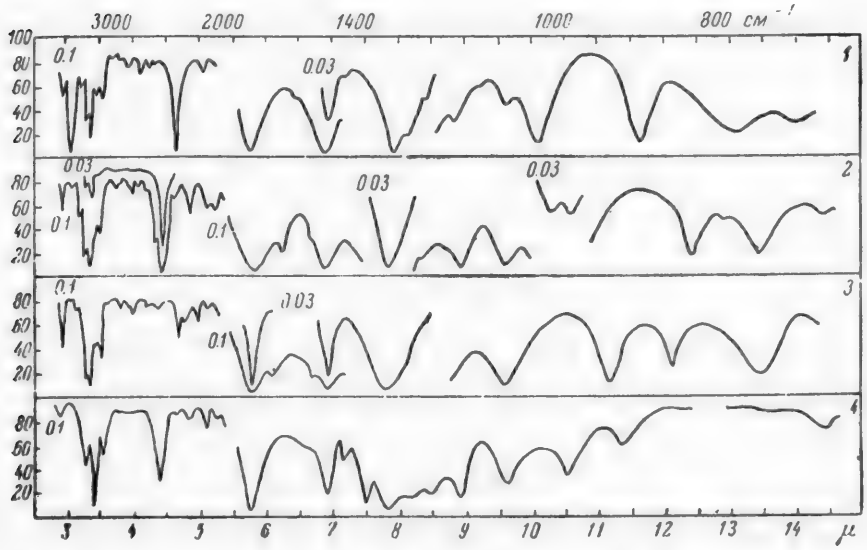


Fig. 2. Infrared transmission spectra. 1) Methyl propiolate; 2) methyl ester of vinylacetylene carboxylic acid; 3) dimethyl ester of acetylene dicarboxylic acid; 4) dibromide of methyl ester of vinylacetylene carboxylic acid.

Infrared spectra were obtained with the IKS-2 spectrometer with an LiF prism in the range up to 5.5 μ and afterwards with an NaCl prism. The spectrum of the dibromide of vinylacetylene carboxylic ester was taken in CCl_4 in comparison with this solvent. Data are presented in the table and Fig. 2.

The rate of bromination of vinylacetylene carboxylic acid ester was investigated in 1% chloroform solution at 22° in the dark and in diffuse light. An equimolar quantity of bromine was taken. The curve of change of concentration of bromine with time is plotted in Fig. 1. The sequence of addition of bromine (judging by the infrared spectrum) is the same in the dark and in the light.

SUMMARY

1. The reaction of the methyl ester of vinylacetylene carboxylic acid with bromine was investigated.

2. On the basis of comparison of the infrared spectra of the dibromide and the original compound, it was shown that the reaction goes preferentially at the double bond.

3. Some of the main regularities in the infrared spectrum of the methyl ester of vinylacetylene carboxylic acid were analyzed.

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*Original Russian pagination. See C. B. translation.

OXIDATION OF VINYLACETYLENIC HYDROCARBONS BY ORGANIC HYDROPEROXIDES

V. OXIDATION OF 6,9-DIMETHYL-5,9-TETRADECADIEN-7-YNE, 4,7-DIMETHYL-3,7-DECADIEN-5-YNE AND 3,6-DIETHYL-2,6-OCTADIEN-4-YNE BY ACETYL HYDROPEROXIDE

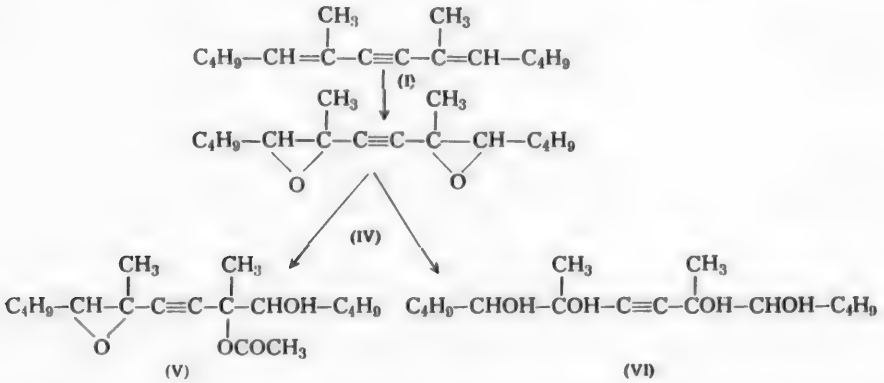
N. M. Malenok, S. D. Kul'kina and Z. Iu. Kovtunenko

In the oxidation by acetyl hydroperoxide of divinylacetylenic hydrocarbons containing the olefinic bonds in the α-position to the triple bond, $-C=C-C\equiv C-C=C-$, dioxides are formed but the triple bond remains intact and its presence is confirmed by bromination.

For further confirmation of this fact, previously established by us [1], we subjected three divinylacetylenic hydrocarbons to oxidation: 6,9-dimethyl-5,9-tetradecadien-7-yne (I), 4,7-dimethyl-3,7-decadien-5-yne (II) and 3,6-diethyl-2,6-octadien-4-yne (III). These hydrocarbons were prepared by dehydration of the corresponding γ-acetylenic glycols.

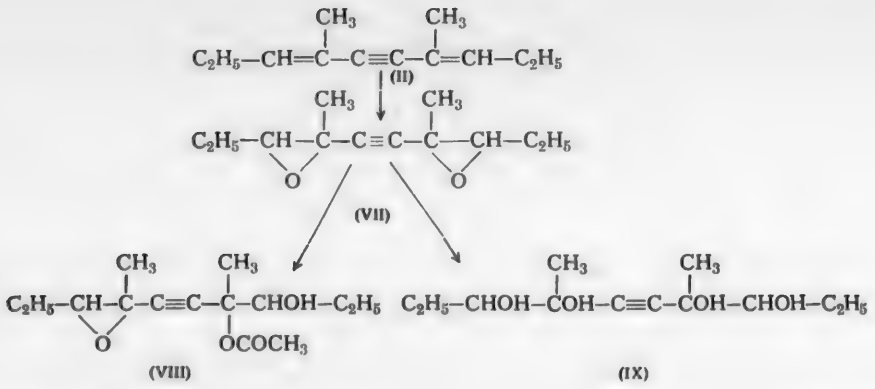
Oxidation of hydrocarbon (I) by acetyl hydroperoxide gave us 6,9-dimethyl-5,9-diepoxy-7-tetradecyne (IV) as the main product, together with the monohydroxide – 6,9-dimethyl-9-acetoxy-5-epoxy-7-tetradecyn-10-ol (V) which is a secondary product resulting from reaction of the dioxide (IV) with acetic acid. This is confirmed by the fact that acetylene dioxides directly form monoxides – alcohol-acetates [2] – on heating with glacial acetic acid.

Hydrolysis of (IV) with 1% sulfuric acid gave the erythritol, 6,9-dimethyl-7-tetradecyn-5,6,9,10-tetralol (VI).



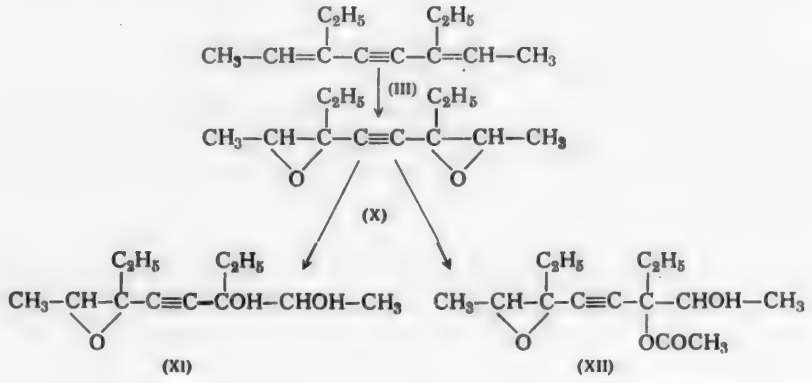
Oxidation of hydrocarbon (II) by acetyl hydroperoxide gave two substances: a dioxide – 4,7-dimethyl-3,7-diepoxy-5-decyne (VII) – and a monoxide – 4,7-dimethyl-7-acetoxy-3-epoxy-5-decyn-8-ol (VIII). The latter is likewise a secondary reaction product resulting from the reaction of the dioxide (VII) with acetic acid.

Hydrolysis of dioxide (VII) gives the erythritol, 4,7-dimethyl-5-decyn-3,4,7,8-tetralol (IX).



(VIII) (IX)

Oxidation of the dienynic hydrocarbon (III) by acetyl hydroperoxide gave three substances: a dioxide, 3,6--diethyl-2,6-diepoxy-4-octyne (X); a monoxide, 3,6-diethyl-2-epoxy-4-octyn-6,7-diol (XI); and another monoxide, 3,6-diethyl-6-acetoxy-2-epoxy-4-octyn-7-ol (XII). The last two substances (XI and XII) are secondary products resulting from reaction of the dioxide (X) with water and with acetic acid:



(XI) (XII)

EXPERIMENTAL

Synthesis of 6,9-dimethyl-7-tetradecyn-6,9-diol. The acetylenic γ-glycol was obtained from methyl amyl ketone (b.p. 148-151°) and ethynyl magnesium bromide in a medium of absolute ether. After recrystallization from methyl alcohol it melted at 86-86.5° [3].

Preparation of 6,9-dimethyl-5,9-tetradecadien-7-yne (I). 45.5 g of the acetylenic glycol was heated in vacuo (30 mm) with 18 g of anhydrous potassium bisulfate until water (split off from the glycol) ceased to distil over. The product was extracted with ether, washed with water and sodium carbonate solution, and dried with potassium carbonate. The ether was then distilled off to leave 38.9 g (80%) of hydrocarbon (I) [3] with b.p. 111--115° (2 mm) $n^{20}D$ 1.4855.

Oxidation of 6,9-dimethyl-5,9-tetradecadien-7-yne (I) by acetyl hydroperoxide. 87.7 g of hydrocarbon dissolved in anhydrous ethyl ether was placed in a freezing mixture (−8°). To the solution was gradually added 77.1 g of 80.5% acetyl hydroperoxide (2 moles hydroperoxide per mole hydrocarbon) likewise previously diluted with anhydrous ether. The rate of addition of acetyl hydroperoxide to the hydrocarbon was so regulated that the temperature of the reaction mixture did not rise above −3°. After the whole of the hydroperoxide had been added, the mixture was stood at room temperature.

The progress of oxidation was followed by titration of the reaction mixture and checking of the experiment with 0.1 N thiosulfate solution. For this purpose, 20 ml each of experimental solution (previously diluted 100 times with water) and test solution were taken, and the amount of unreacted acetyl hydroperoxide was determined iodometrically. Results are presented in Table 1 which shows that the oxidation of 6,9-dimethyl-5,9-tetradecadien-

-7-yne (I) by acetyl hydroperoxide proceeded over a period of 9 days. The concentration of hydroperoxide in the control experiment after this period changed to an insignificant extent (Table 1).

TABLE 1

Type of experiment	Amount of 0.1 N thiosulfate consumed in titration of unreacted acetyl hydroperoxide (in ml)									
	Days									
	1	2	3	4	5	6	7	8	9	10
Main	7.30	1.65	1.25	1.00	0.80	0.70	0.60	0.55	0.40	0.40
Control	7.30	7.30	7.30	7.30	7.30	7.20	7.20	7.20	7.20	7.20

After 10 days the reaction mixture was neutralized with 10% sodium carbonate solution and washed once with water. The ether layer was collected and dried with sodium sulfate; the ether was driven off and the residue fractionally distilled three times to give two substances: 1) b.p. 116-117° (0.5 mm), 36 g; 2) b.p. 160-164° (0.5 mm), 3 g.

The substance with b.p. 116-117° (0.5 mm) is a greenish-yellow liquid, soluble in organic solvents, insoluble in water. It slowly releases iodine from an acidified aqueous solution of potassium iodide, slowly decolorizes a chloroform solution of bromine, does not give a reaction for active hydrogen with methyl magnesium iodide, and gives a negative reaction for the ketone group.

$n^{20}D$ 1.4578, d^{20}_{20} 0.9098, MR_D 74.95; calc. 74.37.

Found %: C 76.51, 76.44; H 10.37, 10.49. M 236.5. $C_{18}H_{26}O_2$. Calculated %: C 76.80; H 10.40. M 250.

The substance is the dioxide, 6,9-dimethyl-5,9-epoxy-7-tetradecyne (IV).

The compound with b.p. 160-164° (0.5 mm), $n^{20}D$ 1.4809 is a very viscous, poorly mobile liquid, soluble in the same solvents as the dioxide.

Found %: C 70.79, 70.63; H 9.97, 10.07. M 322. $C_{18}H_{30}O_4$. Calculated %: C 69.68; H 9.68. M 310.

The compound analyzed is the monoxy-alcohol-acetate, 6,9-dimethyl-9-acetoxy-5-epoxy-7-tetradecyn--10-ol (V). The analytical data indicate that this compound is insufficiently pure; it is evidently contaminated with dioxide.

Hydrolysis of 6,9-dimethyl-5,9-diepoxy-7-tetradecyne (IV). 4.7 g of the dioxide was boiled for 4 hours (frequent vigorous stirring) with 35 ml of 1% H_2SO_4. The upper layer thickened. The aqueous acidic layer was separated; the viscous layer was dissolved in ether and at the same time the ether-insoluble erythritol came down in the form of crystals. The latter were filtered, washed with ether 3 times and recrystallized from 40% ethyl alcohol. Yield 0.97 g with m.p. 193-194°.

Found %: C 67.06, 66.97; H 10.51, 10.85. $C_{16}H_{30}O_4$. Calculated %: C 67.13; H 10.48.

The erythritol, 6,9-dimethyl-7-tetradecyn-5,6,9,10-tetralol (VI), is readily soluble in methyl and ethyl alcohols, insoluble in water, benzene and ethyl ether. The number of hydroxyl groups and the molecular weight could not be determined due to its insolubility in the solvents usually employed for these determinations.

Synthesis of 4,7-dimethyl-5-decyn-4,7-diol. The acetylenic γ-glycol was prepared from methyl propyl ketone (b.p. 102-103° at 756 mm) and ethynyl magnesium bromide. M.p. 59° [4].

Dehydration of 4,7-dimethyl-5-decyn-4,7-diol by potassium bisulfate. To 58 g of fused γ-glycol was added 25 g of anhydrous $KHSO_4$. Heating in vacuo (40 mm) led to removal of water which was distilled off for 30 minutes. The reaction product was extracted with ether and dried with calcium chloride. A second fractional

distillation gave 32 g of a light-yellow liquid, soluble in common organic solvents and corresponding to the divinylacetylenic hydrocarbon, 4,7-dimethyl-3,7-decadien-5-yne (II) [4].

B.p. 72-74° (0.5 mm), $n^{20}D$ 1.4878, d^{20}_{20} 0.8155.

Oxidation of 4,7-dimethyl-3,7-decadien-5-yne (II) by acetyl hydroperoxide. 32 g of the hydrocarbon was oxidized in a medium of anhydrous ethyl ether with 42 g of acetyl hydroperoxide (72%) (2 moles of hydroperoxide to 1 mole of hydrocarbon) at 0°. The temperature of the reaction mixture rose to +5°. Iodometric analysis showed that oxidation of the hydrocarbon proceeded for 8 days. Reaction products were isolated under the same conditions as in the first preparation. Two substances were obtained: 1) b.p. 87.5-88° (0.5 mm), 20 g; 2) b.p. 127-129° (0.5 mm), 5 g.

The substance with b.p. 87.5-88° (0.5 mm) is a light-green, mobile liquid with the same properties as dioxide (IV); it is the dioxide, 4,7-dimethyl-3,7-diepoxy-5-decyne (VII).

$n^{20}D$ 1.4565, d^{20}_{20} 0.9388, MR_D 56.23; calc. 55.90.

Found %: C 74.40, 74.30; H 9.38, 9.47. M 192. $C_{12}H_{18}O_2$. Calculated %: C 74.23; H 9.28. M 194.

The substance with b.p. 127-129° (0.5 mm) is a light-yellow, viscous liquid, soluble in organic solvents, insoluble in water.

$n^{20}D$ 1.4690, d^{20}_{20} 1.0202, MR_D 69.34; calc. 68.17.

Found %: C 66.51, 66.59; H 8.50, 8.93. M 256. $C_{14}H_{22}O_4$. Calculated %: C 66.14; H 8.66. M 254.

The data correspond to the monoxy-alcohol-acetate, 4,7-dimethyl-7-acetoxy-3-epoxy-5-decyn-8-ol (VIII).

Hydrolysis of 4,7-dimethyl-3,7-diepoxy-5-decyne (VII). 3 g of the dioxide was hydrolyzed with 1% H_2SO_4 under the same conditions as for the dioxide (IV). The aqueous layer was collected and evaporated to a small bulk on a water bath. The residue thickened on cooling. Ether was added and the mixture was stirred. Crystals came down and were collected and washed with ether 3 times. 0.4 g of erythritol was obtained: 4,7-dimethyl-5-decyn-3,4,7,8-tetralol (IX) with m.p. 157-158°.

Found %: C 62.42, 62.34; H 9.32, 9.28. $C_{12}H_{22}O_4$. Calculated %: C 62.61; H 9.56.

Oxidation of 3,6-diethyl-2,6-octadien-4-yne (III) by acetyl hydroperoxide. The hydrocarbon was prepared by dehydration of 3,6-diethyl-4-octyn-3,6-diol [5] and agreed in properties with the literature data [6]. 67 g of the hydrocarbon (b.p. 68-69° at 0.5 mm) was oxidized in a medium of anhydrous ethyl ether with 90 g of acetyl hydroperoxide (71.9%) (2 moles hydroperoxide to 1 mole hydrocarbon) at 0°. Oxidation proceeded for 15 days as established by iodometric determinations. The reaction products were isolated by the same procedure as for previous preparations. Three substances were isolated: 1) b.p. 85.5-86° (0.5 mm), 42 g; 2) b.p. 125-127° (0.5 mm), 10 g; 3) m.p. 77°, 1.9 g.

The substance with 85.5-86° (0.5 mm) is a light-yellow liquid with the same properties as the previously described dioxides.

$n^{20}D$ 1.4596, d^{20}_{20} 0.9384, MR_D 56.6; calc. 55.9.

Found %: C 74.38, 74.40; H 9.26, 9.22. M 182. $C_{12}H_{18}O_2$. Calculated %: C 74.23; H 9.28. M 194.

The analytical data correspond to the dioxide, 3,6-diethyl-2,6-diepoxy-4-octyn (X).

The substance with b.p. 125-127° (0.5 mm) is a greenish-yellow, viscous liquid. It dissolves in ethyl ether, chloroform, ethyl alcohol and benzene; it is insoluble in water.

$n^{20}D$ 1.4700, d^{20}_{20} 1.0227, MR_D 69.40; calc. 68.17.

Found %: C 66.33, 66.04; H 8.99, 8.94. M 251.4. $C_{14}H_{22}O_4$. Calculated %: C 66.14; H 8.66. M 254.

The analytical data correspond to 3,6-diethyl-6-acetoxy-2-epoxy-4-octyn-7-ol (XII).

The substance with m.p. 77° was isolated after 10-days' standing of the intermediate fraction with b.p. 121-138° (1 mm) obtained on fractional distillation of the product of oxidation of hydrocarbon (III) by acetyl hydroperoxide. It was twice recrystallized from ethyl ether.

Found %: C 67.44, 67.42; H 9.31, 9.35. M 214. $C_{12}H_{20}O_3$. Calculated %: C 67.83; H 9.43. M 212.

The analytical data identify it as the glycol-monoxide, 3,6-diethyl-2-epoxy-4-octyn-6,7-diol (XI).

The presence of a triple bond in the monoxides and dioxides was confirmed by quantitative bromination in chloroform or benzene solution. Results of bromination are presented in Table 2 and 3.

TABLE 2

Monoxide	Weight of monoxide (in g)	Bromine needed for addition to the triple bond (in g)	
		found	calculated
(VIII) 4,7-Dimethyl-7--acetoxy-3-epoxy-5--decyn-8-ol	0.2612	0.3188	0.3290
(XI) 3,6-Diethyl-2-epoxy--4-octyn-6,7-diol	0.1840	0.2731	0.2777
(XII) 3,6-Diethyl-6--acetoxy-2-epoxy-4--octyn-7-ol	0.2450	0.2974	0.3086

TABLE 3

Dioxide	Weight of dioxide (in g)	Bromine needed for addition to the triple bond (in g)	
		found	calculated
(IV) 6,9-Dimethyl-5,9--diepoxy-7-tetradecyne	0.3650	0.4495	0.4672
(VII) 4,7-Dimethyl-3,7--diepoxy-5-decyne	0.4815	0.7584	0.7942
(X) 3,6-Diethyl-2,6--diepoxy-4-octyne	0.1652	0.2616	0.2725

We see from the tables that bromine adds on substantially in the theoretical amount required for addition of four bromine atoms to a triple bond.

SUMMARY

1. We oxidized the divinylacetylenic hydrocarbons, 6,9-dimethyl-5,9-tetradecadien-7-yne, 4,7-dimethyl-3,7-decadien-5-yne, and 3,6-diethyl-2,6-octadien-4-yne with acetyl hydroperoxide and obtained the dioxides of these compounds: 6,9-dimethyl-5,9-diepoxy-7-tetradecyne, 4,7-dimethyl-3,7-diepoxy-5-decyne, 3,6-diethyl--2,6-diepoxy-4-octyne. We also obtained their derivatives: 6,9-dimethyl-9-acetoxy-5-epoxy-7-tetradecyn-10--ol, 4,7-dimethyl-7-acetoxy-3-epoxy-5-decyn-8-ol, 3,6-diethyl-2-epoxy-4-octyn-6,7-diol and 3,6-diethyl-6--acetoxy-2-epoxy-4-octyn-7-ol.

2. The presence of a triple bond in these compounds was confirmed by quantitative bromination.

3. Hydrolysis of the dioxides, 6,9-dimethyl-5,9-diepoxy-7-tetradecyne and 4,7-dimethyl-3,7--diepoxy-5-decyne gave the erythritols, 6,9-dimethyl-7-tetradecyn-5,6,9,10-tetralol and 4,7-dimethyl-5-decyn--3,4,7,8-tetralol.

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*Original Russian pagination. See C. B. translation.

OXIDATION OF VINYLACETYLENIC HYDROCARBONS BY ORGANIC HYDROPEROXIDES

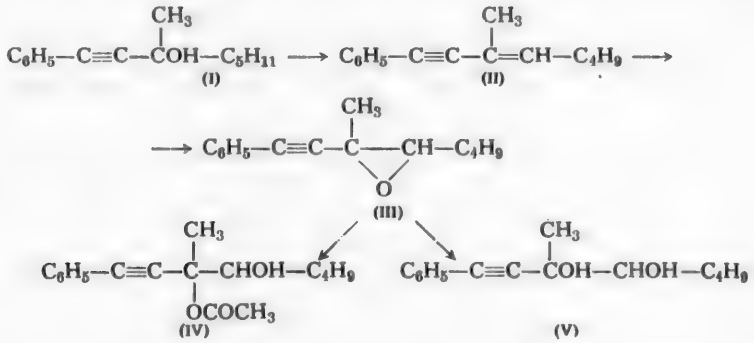
VI. OXIDATION OF 1-PHENYL-3-METHYLOCTEN-3-YNE-1 BY ACETYL HYDROPEROXIDE

N. M. Malenok and S. D. Kul'kina

The present work is a continuation of our investigations on the oxidation of vinylacetylenic hydrocarbons by acetyl hydroperoxide [1, 2].

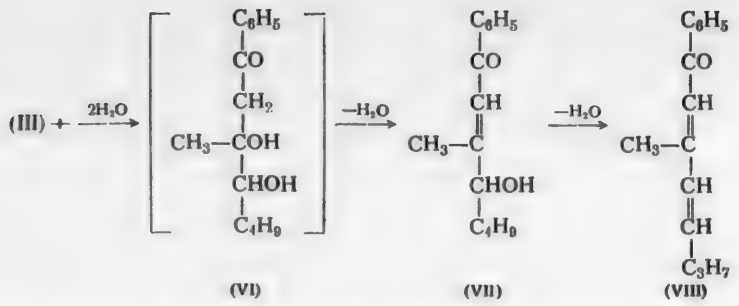
We employed the method of Zh. I. Iotsich to synthesize 1-phenyl-3-methyl-1-octyn-3-ol (I) from ethynylbenzene and methyl amyl ketone. This was dehydrated by potassium bisulfate to the hydrocarbon 1-phenyl-3-methyl-3-octen-yne-1 (II). Oxidation of hydrocarbon (II) by 80% acetyl hydroperoxide gave two substances: the acetylenic oxide, 1-phenyl-3-methyl-3-epoxy-1-octyne (III), and the acetylenic alcohol-acetate, 1-phenyl-3-methyl-3-acetoxy-1-octyn-4-ol (IV). The latter was formed by reaction of oxide (III) with acetic acid. Hydrolysis of oxide (III) by 1% H_2SO_4 gives the acetylenic glycol, 1-phenyl-3-methyl-1-octyn-3,4-diol (V).

The secondary products of the reaction (alcohol-acetates, acetates, glycols) are easily formed if the oxide ring of the acetylenic hydrocarbon is linked to secondary and tertiary or tertiary carbon atoms [1].



We subjected oxide (III) to hydration by the M. G. Kucherov reaction and isolated two substances: an unsaturated ketoalcohol, 1-phenyl-3-methyl-2-octen-4-ol-1-one (VII), and a dienic ketone, 1-phenyl-3-methyl-2,4-octadien-1-one (VIII).

The following mechanism may be advanced for the formation of compounds (VII, VIII). Treatment of oxide (III) with mercuric sulfate solution leads to addition of two molecules of water; one of them adds at the site of rupture of the oxide ring and the second at the acetylenic bond. A ketoglycol – 1-phenyl-3-methyl-3,4-octanediol-1-one (VI) – is presumably first formed; we did not isolate this product. On dehydration, this substance forms the unsaturated ketoalcohol (VII) which on further loss of a molecule of water gives the dienic ketone (VIII).



(VI) (VII) (VIII)

Simultaneous hydration and dehydration by the M. G. Kucherov reaction was first observed by us in the case of 1-phenylethynylcyclohexene-1 oxide [2].

EXPERIMENTAL

Synthesis of 1-phenyl-3-methyl-1-octyn-3-ol (I). The acetylenic alcohol (I) was prepared by the Zh. I. Iotsich reaction from 102 g of ethynylbenzene (b.p. 141-143° at 750 mm) and 114 g of methyl amyl ketone (b.p. 148-151° at 750 mm) in a medium of absolute ether. The compound is a colorless, viscous liquid, soluble in organic solvents. Yield 146.5 g (70%).

B.p. 139.5-140° (0.5 mm), $n^{20}D$ 1.5257, d^{20}_{20} 0.9487, MR_D 69.85; calc. 67.39.

Found %: C 82.92, 83.03; H 9.54, 9.40. M 213.4. $C_{15}H_{20}O$. Calculated %: C 83.33; H 9.26. M 216.

Preparation of 1-phenyl-3-methyl-3-octen-1-yne (II). 75.3 g of alcohol (I) was heated at 30-40° in vacuo (26 mm) with 29 g of anhydrous potassium bisulfate. Dehydration of the alcohol commenced immediately, and the liberated water was distilled off in the course of 10 minutes. The product was extracted with ether and the extract dried with potassium carbonate. The ether was driven off and the residue subjected to two fractional distillations to give 57.3 g (83%) of a light-yellow substance.

B.p. 107-108° (0.5 mm), $n^{20}D$ 1.5465, d^{20}_{20} 0.9114, MR_D 68.95; calc. 65.40.

Found %: C 90.50, 90.57; H 9.32, 9.22. M 198.5. $C_{15}H_{18}$. Calculated %: C 90.91; H 9.09. M 198.

Oxidation of 1-phenyl-3-methyl-3-octen-1-yne (II) by acetyl hydroperoxide. 40.8 g of hydrocarbon (II) was oxidized in a medium of anhydrous ether by 20.4 g of acetyl hydroperoxide (80%) (1 mole of hydroperoxide per mole of hydrocarbon). After the whole of the acetyl hydroperoxide had been added to the substance, the reaction mass was left overnight at room temperature. The course of oxidation of the substance was checked daily by titration with 0.1 N thiosulfate solution. In the first 24 hours 70% of the acetyl hydroperoxide had reacted with the hydrocarbon, and after 10 days the substance was nearly completely oxidized. The reaction product was neutralized with 10% sodium carbonate solution. The ether layer was separated, washed twice with water and then dried with potassium carbonate. The ether was driven off and the residue was subjected to two fractional distillations to give two substances: 1) b.p. 117-118° (0.5 mm), 29.1 g; 2) b.p. 155-156° (0.5 mm), 4 g.

The substance with b.p. 117-118° (0.5 mm) was a greenish-yellow liquid, soluble in organic solvents, insoluble in water. It slowly liberates iodine from potassium iodide solution acidified with sulfuric acid, does not liberate methane when treated with methyl magnesium iodide, and slowly decolorizes a chloroform solution of bromine.

$n^{20}D$ 1.5270, d^{20}_{20} 0.9572, MR_D 68.57; calc. 66.01.

Found %: C 83.91, 83.81; H 8.43, 8.55. M 209. $C_{15}H_{18}O$. Calculated %: C 84.11; H 8.41. M 214.

The properties and analysis of this substance correspond to the acetylenic monoxide – 1-phenyl-3-methyl--3-epoxy-1-octyne (III).

The compound with b.p. 155-156° (0.5 mm) is a viscous, poorly mobile liquid, soluble in ether, ethyl alcohol and chloroform; insoluble in water. It is the alcohol-acetate – 1-phenyl-3-methyl-3-acetoxy-1-octyn-4-ol (IV).

$n^{20}D$ 1.5288, d^{20}_{20} 1.0404, MR_D 81.19; calc. 78.28.

Found %: C 75.25, 75.55; H 7.96, 7.62; OH 6.54. M 262. $C_{17}H_{22}O_3$. Calculated %: C 74.45; H 8.03; OH 6.25; M 274.

Hydrolysis of oxide (III). 2 g of the oxide was boiled with 14 ml of 1% sulfuric acid solution (frequent shaking) for 8 hours. The thickened upper layer was dissolved in ether. The ethereal layer was separated, washed with sodium carbonate solution and then with water, and dried by anhydrous sodium sulfate. The ether was distilled off and the residual mass crystallized on standing. The crystals were dissolved in ethyl alcohol and precipitated from the solution with water. The substance was twice purified in this manner and then had m.p. 81°.

Found %: C 76.28, 76.29; H 9.10, 9.02; OH 14.73. M 239. $C_{15}H_{20}O_2$. Calculated %: C 77.58; H 8.62; OH 14.65. M 232.

The compound is the acetylenic glycol, 1-phenyl-3-methyl-1-octyn-3,4-diol (V).

Hydration of oxide (III) by the M. G. Kucherov reaction. 6 g of the oxide was heated with 22 ml of a solution of mercuric sulfate acidified with sulfuric acid (3.5 g of $HgSO_4$, 2.5 ml of conc. H_2SO_4 and 75 ml of water). At 30° the solution acquired an orange-red color. Increase of temperature to 40° caused the reaction to go very vigorously and the temperature rose further. The reaction mixture was therefore cooled with water and the temperature was not allowed to rise above 40°. A grey precipitate came down after 30 minutes and the reaction was completed. The product was extracted with ether and filtered. The ethereal extract was dried with sodium sulfate. The ether was distilled off, and the residue fractionally distilled three times to give 2.3 g of product.

B.p. 124-126° (4 mm), $n^{20}D$ 1.5581, d^{20}_{20} 0.9913. MR_D 69.62; calc. 66.95.

Found %: C 83.55, 83.43; H 8.76, 8.78. M 204. $C_{15}H_{18}O$. Calculated %: C 84.11; H 8.41. M 214.

The substance rapidly decolorizes bromine in chloroform solution; with 2,4-dinitrophenylhydrazine it forms a red tarry precipitate from which pure crystals could not be isolated; it reacts very weakly with methyl magnesium iodide. It may be suggested that the substance is the dienic ketone, 1-phenyl-3-methyl-2,4-octadiene-1-one (VIII) with a very small admixture of the unsaturated ketoalcohol (VII) which lowers the carbon content and results in a value of 0.15 OH group on analysis.

The presence of two double bonds was proven by bromination of the compound in chloroform.

0.240 g of substance added 0.351 g of bromine. Calculated 0.359 g of bromine for two double bonds.

The last fraction, obtained after isolation of the dienic ketone (VIII), partly crystallized. Recrystallization from aqueous alcohol gave 0.3 g of substance with m.p. 70°.

Found %: C 76.95; H 8.08. M 232.8. $C_{15}H_{20}O_2$. Calculated %: C 77.58; H 8.62. M 232.0.

The substance is clearly the unsaturated ketoalcohol – 1-phenyl-3-methyl-2-octen-4-ol-1-one (VII).

SUMMARY

1. Oxidation of 1-phenyl-3-methyl-3-octen-1-yne by acetyl hydroperoxide gave two substances: the acetylenic oxide, 1-phenyl-3-methyl-3-epoxy-1-octyne, and the alcohol-acetate, 1-phenyl-3-methyl-3-acetoxy--1-octyn-4-ol. Hydrolysis of the oxide gave the acetylenic glycol, 1-phenyl-3-methyl-1-octyn-3,4-diol.

2. Hydration of the oxide by the M. G. Kucherov reaction gave the unsaturated ketoalcohol, 1-phenyl-3--methyl-2-octen-4-ol-1-one, and the dienic ketone, 1-phenyl-3-methyl-2,4-octadien-1-one.

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*Original Russian pagination. See C. B. Translation.

2-PHENYL-3-BROMOBUTENE-2 IN THE GRIGNARD REACTION

V. I. Pansevich-Koliada

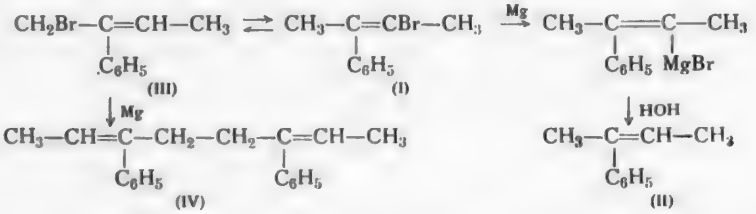
2-Phenyl-3-bromobutene-2 (I) was first prepared by bromination of 2-phenylbutene-2 (II) [1]. The same bromide is also formed on bromination of 2-phenylbutanol-2 in anhydrous solvents [2].

The action of alcoholic alkali on 2-phenyl-3-bromobutene-2 leads to the unsaturated ether 2-phenyl-4--ethoxybutene-2 [3]. The reaction goes with great facility, which indicates the great mobility of the halogen at the double bond of compound (I).

In the present work we studied the behavior of 2-phenyl-3-bromobutene-2 (I) in the Grignard reaction. Reaction starts at once when bromide (I) is added to magnesium in ether, and it goes vigorously to completion, but only one-half of the magnesium reacts. Decomposition of the reaction mixture by water proceeds with scarcely any liberation of heat, in contrast to the behavior of the usual organomagnesium compounds. The main product of the reaction was a hydrocarbon with the empirical formula $C_{20}H_{32}$ (IV), i.e., the carbon skeleton of the bromide (I) is doubled. The hydrocarbon 2-phenylbutene-2 (II) was found in the 1st fraction; it is always formed in small quantity.

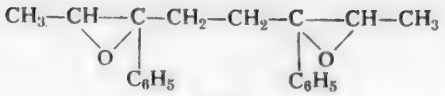
The structure of hydrocarbon (IV) was confirmed by oxidation of potassium permanganate, potassium dichromate and chromic anhydride. Diphenacyl and acetic acid were found in all cases in the reaction products. The same substances were also obtained on decomposition of the ozonide of the hydrocarbon (IV). Formation of diphenacyl and acetic acid in the present case could only proceed through oxidation of 3,6-diphenyloctadiene--2,6 (IV), so that the latter, contrary to our earlier suggestion [4], is the main product of the reaction of 2-phenyl--3-bromobutene-2 (I) with magnesium.

Formation of hydrocarbon (IV) undoubtedly proceeds through a series of intermediate processes during reaction of magnesium with bromide (I). In ethereal solution a tautomeric transformation occurs between 2-phenyl--3-bromobutene-2 (I) and its isomer (formed in solution) – 2-phenyl-1-bromobutene-2 (III). Bromide (III), like other halides of the allylic type [5-8], undergoes a Wurtz reaction with magnesium to form 3,6-diphenyloctadiene--2,6 (IV). Bromide (III) reacts quickly with magnesium and this is therefore the main direction of reaction. At the same time the normal reaction of magnesium with bromide (I) takes place to a very small extent and leads to hydrocarbon (II). The processes can be represented by the equations:



In the present case the isomeric transformation of the bromides (I and III) is similar to the well-known isomeric transformation of chlorobutenes-2 [9].

We oxidized 3,6-diphenyloctadiene-2,6 (IV) by acetyl hydroperoxide. The resultant dioxide – 3,6-diphenyl--2,3,6,7-diepoxyoctane (V) – is unstable and undergoes slight modification on distillation in vacuo.



(V)

EXPERIMENTAL

Preparation of 3,6-diphenyloctadiene-2,6 (IV). The starting bromide (I) was prepared by the action of bromine on 2-phenylbutanol-2 in chloroform [2].

B.p. 118-120° (11 mm), $n^{20}D$ 1.5811, d^{20}_4 1.3348, MR_D 52.66; calc. 52.08.

40 g of bromide (I) was added gradually (with progressive entry into reaction) to 20 g of magnesium turnings in ether. The reaction started quickly and proceeded vigorously to the end. After the whole of the bromide had been added, the mixture was heated on a water bath for an hour. When the reaction was completed, the mixture was homogeneous, andonly after standing overnight did a very small quantity of stout crystals form on the walls of the flask. The reaction mixture was decomposed by water; very slight heat development occurred on addition of the water. The ether layer was separated, the aqueous layer was extracted with ether and the extract added to the ether layer which was then dried with $MgSO_4$. After removal of the ether, the reaction products were distilled to give the following fractions: 1st, 40-139°, 6.1 g; 2nd, 130-155°, 0.8 g; 3rd, 155-158°, 16.2 g; 4th, 158-165°, 1.0 g; a small residue remained in the flask.

The 3rd fraction was redistilled to give 14.9 g of hydrocarbon (IV) in the form of a yellowish, oily and slightly opalescent liquid.

B.p. 156-157° (2 mm); $n^{20}D$ 1.5750, d^{20}_4 0.9880, MR_D 87.63; calc. 86.42.

Found %: C 91.06; H 8.57; M 247.7, 250.9. $C_{20}H_{22}$. Calculated %: C 91.22; H 8.78. M 262.

Redistillation of the 1st fraction gave a colorless, mobile liquid in a quantity of 2 g; this was 2-phenylbutene--2 (II).

B.p. 46.5 -48° (3 mm), $n^{20}D$ 1.5962, d^{20}_4 0.9156, MR_D 44.03; calc. 44.31.

Oxidation of 3,6-diphenyloctadiene-2,6 (IV) by chromic anhydride. 3 g of the hydrocarbon was dissolved in 15 ml of glacial acetic acid and 4 g of chromic oxide in 30 ml of glacial acetic acid was gradually added (cooling to 5-10°). Oxidation was energetic. The reaction mixture was diluted with water and the reaction products extracted with a mixture of ether and benzene. The solvent was distilled off to leave 0.35 g of crystalline substance, poorly soluble in ether, very poorly soluble in chloroform, and more soluble in benzene. The compound does not contain active hydrogen; when dissolved in concentrated sulfuric acid it forms a green solution which becomes reddish-brown with a green fluorescence when gently heated. M.p. 145.5-146.5° (from benzene).

Found %: C 80.56; H 6.21. M 221.6. $C_{16}H_{14}O_2$. Calculated %: C 80.67; H 5.88. M 238.

The data correspond to diphenacyl [10]. The semicarbazide was prepared; m.p. 199-201° (from ethyl alcohol).

Oxidation of 3,6-diphenyloctadiene-2,6 by permanganate and dichromate in an aqueous medium goes very slowly due to its extremely poor solubility in water. The reaction products were diphenacyl, benzoic acid (m.p. 121°) and acetic acid; the silver salt of the latter was prepared.

Found %: Ag 65.02. $C_2H_3O_2Ag$. Calculated %: Ag 64.64.

Benzoic acid was undoubtedly formed by oxidation of the diphenacyl.

Oxidation of 3,6-diphenyloctadiene-2,6 (IV) by ozone. 3 g of the hydrocarbon was dissolved in 20 g of chloroform and ozonized oxygen was passed through.* The chloroform was distilled off in vacuo without heating. An oily ozonide and a small amount of crystals remained in the flask. Water was added to the ozonide, and the flask contents were refluxed on a boiling water bath for 6 hours. The aqueous solution had an acid reaction. The acids were neutralized with water, and the neutral reaction products were extracted with ether-benzene mixture.

*It should be remarked that the reaction mixture caught fire when an attempt was made to ozonize this hydrocarbon in hexane.

The solvents were distilled off to leave colorless crystals which after recrystallization from benzene melted at 146-147°. No depression of melting point was observed in a mixed test with the crystals obtained on oxidation of 3,6-diphenyloctadiene-2,6 by chromic anhydride.

The salts of the acids were decomposed with sulfuric acid and the volatile acids were distilled off with steam by boiling the solution of the acids. The first portions of the distillate gave a silver salt of a volatile acid on treatment with silver carbonate.

Found %: Ag 64.25. $C_2H_3O_2Ag$. Calculated %: Ag 64.64.

Consequently, decomposition of the ozonide had given diphenacyl and acetic acid. No other products were detected.

Oxidation of 3,6-diphenyloctadiene-2,6 (IV) by acetyl hydroperoxide. To 60 g of hydrocarbon dissolved in 100 ml of absolute ether was added 100 g of 38% acetyl hydroperoxide at 20-28°. Oxidation was completed in 7 days. The acetic acid was washed out with water, and the ethereal solution was dried with sodium sulfate. Distillation (3 mm) of the oxidation products gave the following fractions: 1st, up to 193°, 15 g; 2nd, 193-197°, 29 g; 3rd, 197-204°, 9 g. Each fraction was a viscous, noncrystallizing oil with a light-yellow color and possessing an odor of active oxygen. The compound dissolved in benzene, chloroform, acetone and other organic solvents.

Found %: C 79.04; H 7.64. M 280.5, 284.5. $C_{20}H_{22}O_2$. Calculated %: C 81.59; H 7.48. M 294.

The dioxide (VI) was contaminated with some other substance containing active hydrogen. Redistillations of the dioxide resulted in progressive lowering of the percentage of carbon, due undoubtedly to slight decomposition of the dioxide at its fairly high boiling point. Derivatives of dioxide (VI) could not be prepared.

SUMMARY

1. Reaction of 2-phenyl-3-bromobutene-2 with magnesium in ether gives mainly 3,6-diphenyloctadiene--2,6.

2. Oxidation of 3,6-diphenyloctadiene-2,6 by acetyl hydroperoxide gives a dioxide — 3,6-diphenyl-2,3--6,7-diepoxyoctane — which partly decomposes on distillation due to its high boiling point.

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Belorussian Polytechnic Institute

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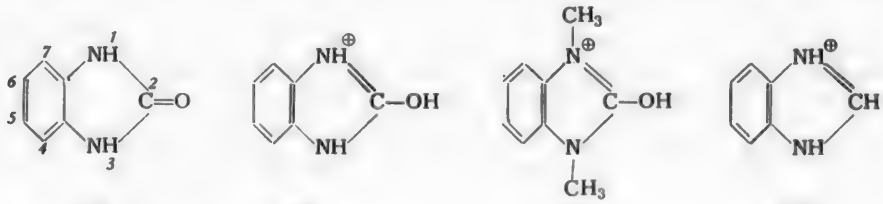
INVESTIGATIONS ON IMIDAZOLE DERIVATIVES

XIX. AMINO DERIVATIVES OF BENZIMIDAZOLONE AND 1,3-DIMETHYLBENZIMIDAZOLONE

L. S. Efros and A. V. El'tsov

It was shown earlier [1, 2] that in a strongly acidic medium benzimidazolone (I) and its N,N'-dimethyl derivative do not differ in reactivity and spectral absorption from derivatives of benzimidazole. This justifies the assumption that during salt formation a proton joins on at their carbonyl oxygen with formation of cations (II) and (III).



(I) (II) (III) (IV)

The upsetting of the equivalence of the single and double bonds in the benzene ring of such cations is comparable with that in naphthalene [3].

In a neutral medium, however, benzimidazolone exists in the o-phenyleneurea form [2], and therefore, its heteroring differs from the imidazole ring. For this reason it appeared to us of interest to study the effect of the imidazolone ring on the benzene ring condensed with it and to attempt to establish the character of the deformation of the electron cloud in the latter.

With this objective we undertook an investigation of the chemical properties of the isomeric 4- and 5-amino derivatives of both benzimidazolone and its 1,3-dimethyl analog. The latter are not less interesting because similarity between their reactivity and that of derivatives of unmethylated benzimidazolone could serve as yet another proof of the o-phenyleneurea structure of benzimidazolone.

We prepared the amines by reduction of the corresponding nitro derivatives with tin and conc. hydrochloric acid. The free amines are easily oxidized by atmospheric oxygen, and we therefore preferred to work with their hydrochlorides.

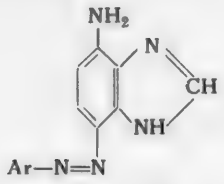
It was found that 4-aminobenzimidazolone and its 1,3-dimethyl analog are very much less basic than the corresponding 5-amino derivatives. A similar difference in basic properties was also observed in the series of the isomeric 4- and 5-aminobenzimidazoles [4] (Table 1). These substances react differently with diazonium salts.

TABLE 1

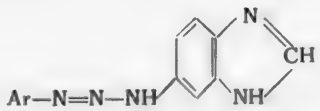
Compound	pK_{base}*
4-Aminobenzimidazolone	10.76
5-Aminobenzimidazolone	9.00
4-Amino-1,3-dimethylbenzimidazolone	10.94
5-Amino-1,3-dimethylbenzimidazolone	9.11

* The basicity constants were measured with a LP-4 lamp potentiometer with a pH electrode at the point of half-equivalence at 18°.

4-Aminobenzimidazole entered smoothly into the azo-coupling reaction and formed an azo dye with the azo group at the carbon atom in the 7-position (V); 5-aminobenzimidazole only formed diazoamino compounds (VI) on reaction with diazotized aromatic amines.



(V)

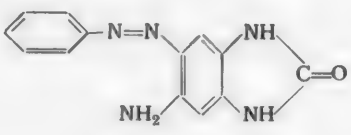


(VI)

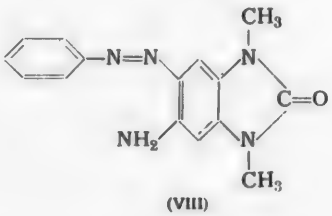
The isomeric 4- and 5-aminobenzimidazolones that we synthesized behaved in exactly the opposite manner: 5-aminobenzimidazolone and its 1,3-dimethyl analog readily entered into the azocoupling reaction with diazotized aniline, whereas the 4-amino derivative only coupled with diazotized p-nitroaniline, and formed a diazoamino compound with the less active diazo component.

It was very important to establish the position in the molecule where 5-aminobenzimidazolone enters into the azocoupling reaction. The azo dye, obtained by coupling 5-aminobenzimidazolone with diazotized aniline, was reduced with tin in hydrochloric acid, and the mixture of reduction products was treated with an aqueous solution of the bisulfite derivative of phenanthrenequinone. After the separated phenanthrazine had been recrystallized, its absorption spectrum in concentrated sulfuric acid showed it to be identical with the phenanthrazine obtained from 5,6-diaminobenzimidazolone [5, 6] (Fig. 1).* We obtained the same results in the case of the dye from 5-amino-1,3-dimethylbenzimidazolone and diazotized aniline.

Consequently, azocoupling of 5-aminobenzimidazolone and its 1,3-dimethyl derivative takes place at the carbon atom in the 6-position with formation of azo dyes (VII) and (VIII) respectively.



(VII)

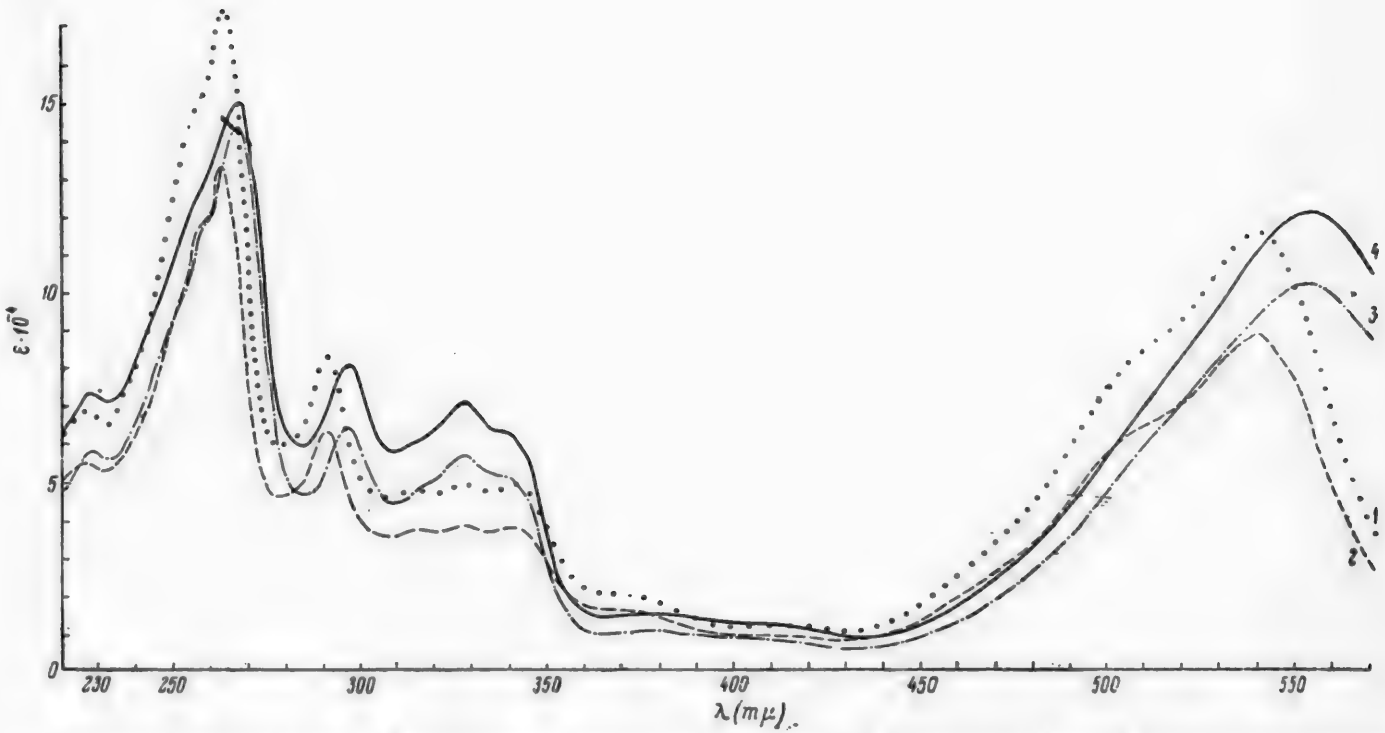


(VIII)

The identical chemical behavior of the amino derivatives both of the unsubstituted benzimidazolone and of its 1,3-dimethyl analog bears witness to the identical influence of the heterorings of these compounds on the benzene rings condensed with them and, consequently, also bears witness to the sameness of structure of the heterorings themselves, as was demonstrated earlier by other methods [2].

The observed facts enable us to assume that in 5-aminobenzimidazolone as well as in its 1,3-dimethyl derivative, the equivalence of the bonds of the benzene ring is upset, the double-bond character in the 5,6-position being sharply increased (I). The consequence is that azocoupling of the 5-amino derivatives occurs in the 6-position. If this hypothesis is correct, then a similar deformation of the electron cloud occurs in the benzene ring of the unsubstituted benzimidazolone, for otherwise it would be difficult to account for the differing reactivities of 5-aminobenzimidazole and 5-aminobenzimidazolone. It should be noted that destruction of bond equivalence of this type is of general interest since it had never previously been observed except in the case of hydrindene [7], and the conclusions drawn from this are now considered to be erroneous [8].

* The absorption spectra were prepared with the SF-4 spectrophotometer in screw-top quartz cells with a layer thickness of 0.5 cm and solution concentrations of 2×10^{-5} to 7×10^{-5} mole/liter. The slight differences in the extinction coefficients, in spite of the complete identity in the absorption character, can be attributed to experimental errors due to the low concentrations of the solutions.



Ultraviolet absorption spectra of phenanthrazines in concentrated sulfuric acid. 1) Phenanthrazine from 5,6-diaminobenzimidazolone; 2) phenanthrazine from products of reduction of 5-amino-6-(phenylazo)-benzimidazolone; 3) phenanthrazine from 5,6-diamino-1,3-dimethylbenzimidazolone; 4) phenanthrazine prepared from products of reduction of 5-amino-6-(phenylazo)-1,3-dimethylbenzimidazolone.

EXPERIMENTAL

4-Nitro-1,3-dimethylbenzimidazolone. 3.1 g of 4-nitrobenzimidazolone was dissolved in 70 ml of 4% NaOH, and dropwise addition was made to the stirred solution (heated to 80°) of 3.4 ml of dimethyl sulfate; thereupon 10 ml of 30% NaOH was added and the solution was stirred at the boil for 10 minutes. Another 3.4 ml of dimethyl sulfate was then added and very little solid alkali, and the solution was stirred at the boil for 30 minutes. The precipitate was filtered from the hot solution and washed with water. Yield of unpurified product 30%.

Incompletely methylated products separate from the mother liquor on acidification and can be again subjected to methylation. After recrystallization from acetic acid, the substance has the form of fine, lustrous, greenish-yellow crystals, melting at 190-192.5°.

Found %: C 52.44; H 4.00; N 20.27. $C_9H_9O_3N_3$. Calculated %: C 52.17; H 4.38; N 20.28.

The amino derivatives of benzimidazolone and 1,3-dimethylbenzimidazolone were synthesized by reduction of the nitro products. The nitro product was added in small portions to a previously heated mixture of granulated tin and concentrated hydrochloric acid. The reaction went fairly vigorously and was accompanied by considerable evolution of heat. After completion of the reduction reaction, the hot solution was decanted from the tin residues and cooled. The precipitated complex salt of the amine was filtered and dissolved in a suitable quantity of water; the tin was brought down from the solution by hydrogen sulfide, the tin sulfide was filtered off and the mother liquor was evaporated to dryness in a dish on a water bath. The hydrochloride of the amine was purified. The hydrochlorides of the amines do not melt or decompose sharply.

4-Aminobenzimidazolone hydrochloride. Reactants were 36 g of 4-nitrobenzimidazolone, 175 ml of concentrated hydrochloric acid and 70 g of tin. The amine hydrochloride was purified by dissolution in hot water, treatment with animal charcoal and dilution with concentrated hydrochloric acid. The precipitate was filtered off and dried at 60-70°. Yield 23 g of heavy, colorless needles.

Found %: C 44.88; H 4.57; N 22.54, 22.79; Cl 19.25. $C_7H_7ON_3 \cdot HCl$. Calculated %: C 45.29; H 4.34; N 22.64; Cl 19.10.

The picrate melts at 241° with decomposition.

4-Amino-1,3-dimethylbenzimidazolone hydrochloride. Reactants were 2.3 g of 4-nitro-1,3-dimethylbenzimidazolone, 4 g of tin, and 20 ml of concentrated hydrochloric acid. The yield of hydrochloride was 75%. It crystallizes from water as long, colorless needles containing water of crystallization.

Found %: C 46.84; H 5.88; N 18.28. $C_9H_{11}ON_3 \cdot HCl \cdot H_2O$. Calculated %: C 46.66; H 6.10; N 18.14.

5-Amino-1,3-dimethylbenzimidazolone hydrochloride. Reactants were 6.1 g of 5-nitro-1,3-dimethylbenzimidazolone [1], 10.5 g of tin, and 40 ml of concentrated hydrochloric acid. The yield of amine hydrochloride was 80%. The salt was purified by crystallization from alcohol with addition of concentrated hydrochloric acid. Colorless, microscopic needles containing one molecule of water.

Found %: C 47.05; H 5.84; N 18.01; Cl 15.56, 15.61. $C_9H_{11}ON_3 \cdot HCl \cdot H_2O$. Calculated %: C 46.66; H 6.10; N 18.14; Cl 15.30.

Coupling of 4-aminobenzimidazolone with diazotized p-nitroaniline. A solution of 0.43 g of 4-aminobenzimidazolone hydrochloride in 10 ml of water was stirred into a solution of 0.55 g of p-nitrophenyldiazonium fluoborate in 30 ml of water. The precipitate was filtered off, twice recrystallized from aqueous pyridine, treated with boiling 2% acetic acid, washed with water, and dried. A dark-grey powder, melting unsharply at 298° with decomposition.

Found %: N 28.12, 28.32. $C_{13}H_{10}O_3N_6$. Calculated %: N 28.18.

5-Amino-6-(phenylazo)-benzimidazolone. To a cooled solution (0°) of 7 g of 5-aminobenzimidazolone hydrochloride in 150 ml of water was added, with stirring, a solution of diazotized aniline (prepared in the usual manner) in the theoretical quantity. An excess of sodium acetate was then added, and the precipitated azo dye was filtered after 30 minutes. Purification was effected by reprecipitation from alkali with acetic acid. The product was reduced.

A sample for analysis was obtained by crystallizing part of the product from 4% aqueous sodium carbonate

solution and then from dilute hydrochloric acid. The hydrochloride of 5-amino-6-(phenylazo)-benzimidazolone is a black, amorphous powder which does not melt at 325°.

Found %: N 24.11, 24.16. $C_{13}H_{11}ON_5 \cdot HCl$. Calculated %: N 24.18.

5-Amino-6-(phenylazo)-1,3-dimethylbenzimidazolone. Excess of sodium acetate was stirred into a solution, cooled to 0°, of 7 g of 5-amino-1,3-dimethylbenzimidazolone hydrochloride in 150 ml of water; a solution of aniline diazotized in the usual manner was then added in the theoretical quantity. The precipitated azo dye was filtered after 30 minutes and subjected to reduction without purification.

The same dye was prepared for analytical purposes by running together solutions of 0.96 g of the amine hydrochloride in 40 ml of water and of 0.8 g of the fluoborate of diazotized aniline in 30 ml of water. Sodium acetate was added to the mixture and the precipitated dye was filtered off. The precipitate was recrystallized from dilute hydrochloric acid. 5-Amino-6-(phenylazo)-1,3-dimethylbenzimidazolone hydrochloride is a black, amorphous powder without a sharp melting point and decomposing at 245°.

Found %: N 22.31, 22.13. $C_{15}H_{15}ON_5 \cdot HCl$. Calculated %: N 22.04.

Reduction of the azo dyes of the 5-amino derivatives was effected with tin in concentrated hydrochloric acid. The reaction mass was diluted with water, the tin was brought down with hydrogen sulfide, the tin sulfide was filtered off, and the solution was evaporated to dryness in vacuo. The dry salt was dissolved in water and excess of the bisulfite compound of phenanthrenequinone was added to the solution. After 5 hours, the precipitated phenthrazine was filtered off and crystallized from a suitable solvent.

The phenanthrazine from 5-amino-6-(phenylazo)-benzimidazolone was crystallized from aqueous pyridine and then treated with 2% boiling aqueous acetic acid. A yellow powder, not melting at 320°. Very sparingly soluble in organic solvents; can be recrystallized from a large volume of acetic acid. Gives a bright crimson color with concentrated sulfuric acid.

Found %: N 16.94, 16.95. $C_{21}H_{12}ON_4$. Calculated %: N 16.66.

The phenanthrazine from 5-amino-6-(phenylazo)-1,3-dimethylbenzimidazolone crystallized from a large volume of dioxan ; a yellow powder; gives a bright crimson color with concentrated sulfuric acid.

Found %: N 15.37, 15.59. $C_{23}H_{16}ON_4$. Calculated %: N 15.38.

5,6-Diamino-1,3-dimethylbenzimidazolone. Reaction components were 6.3 g of 5,6-dinitro-1,3-dimethylbenzimidazolone [1], 20 g of tin and 45 ml of concentrated hydrochloric acid. The hydrochloride of the diamine is very easily soluble in water and is not salted out by concentrated hydrochloric acid. The free base can be isolated by addition of sodium acetate to a concentrated aqueous solution of the hydrochloride. It forms a colorless powder, very sparingly soluble in organic solvents. Its melting point is above 320°. Small quantities of moisture promote oxidation of the diamine by atmospheric oxygen, so that it must be stored in a vacuum-desiccator over P_2O_5.

The diamine was identified through its phenanthrazine whose absorption spectrum and elemental composition corresponded to the phenanthrazine prepared from 5-amino-6-(phenylazo)-1,3-dimethylbenzimidazolone.

5,6-Diaminobenzimidazolone was prepared earlier [5, 6]. We synthesized it in 70% yield by reduction of 5,6-dinitrobenzimidazolone with tin and concentrated hydrochloric acid. The diamine was converted by the method described above into the phenanthrazine, whose absorption spectrum and elemental composition identified it with the phenanthrazine from 5-amino-6-(phenylazo)-benzimidazolone.

SUMMARY

5-Aminobenzimidazolone and its 1,3-dimethyl derivative differ from 5-aminobenzimidazole by entering into the azocoupling reaction. This leads to an azo dye containing the azo group in the 6-position. This direction of the azocoupling reaction may serve as proof of the presence in the benzene ring of benzimidazolone of an intensified double-bond character between carbon atoms 5 and 6.

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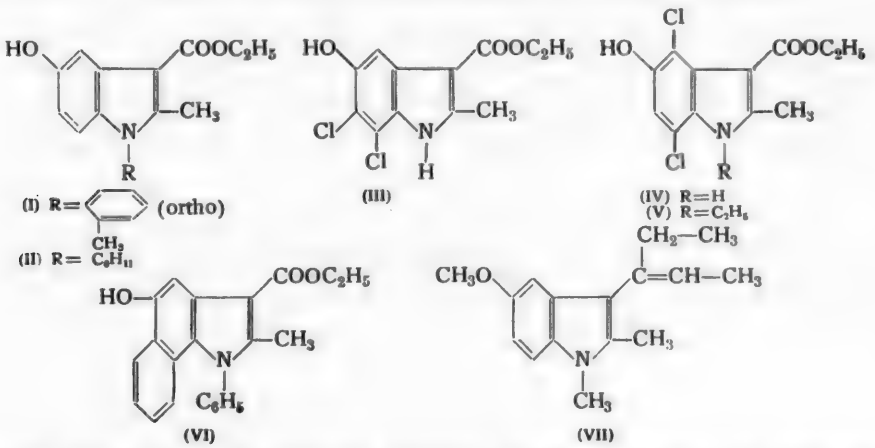
INVESTIGATIONS ON QUINONES

XXII. THE SYNTHESIS OF SUBSTITUTED INDOLES

A. N. Grinev, I. A. Zaitsev, V. I. Shvedov and A. P. Terent'ev

Reaction of p-quinones with esters of β-aminocrotonic acid and its closest analogs leads, as we know, to 5-hydroxy-substituted indoles and benzindoles [1-4]. Our investigations also revealed that imines of acetylacetone react in two ways with p-benzoquinone to give either substituted indoles [3, 5] or benzofurans [4, 5].

We have now succeeded in broadening the scope of this reaction somewhat. Condensation of ethyl β-aminocrotonate and some of its analogs with p-benzoquinone, 2,3-dichloro-p-benzoquinone, 2,5-dichloro-p-benzoquinone and α-naphthoquinone gave the ethyl ester of 1-(o-tolyl)-2-methyl-5-hydroxyindole-3-carboxylic acid (I), the ethyl ester of 1-cyclohexyl-2-methyl-5-hydroxyindole-3-carboxylic acid (II), the ethyl ester of 2-methyl-5-hydroxy-6,7-dichloroindole-3-carboxylic acid (III), the ethyl ester of 2-methyl-4,7-dichloro-5-hydroxyindole-3-carboxylic acid (IV), the ethyl ester of 1-ethyl-2-methyl-4,7-dichloro-5-hydroxyindole-3-carboxylic acid (V) and the ethyl ester of 1-phenyl-2-methyl-5-hydroxybenzoindole-3-carboxylic acid (VI).



In addition, we studied the transformations of substituted indoles – methylated and benzoylated hydroxyindoles prepared in the present work and in preceding studies [2-6] – and the interaction of the ethyl ester of 1,2-dimethyl-5-methoxyindole-3-carboxylic acid with ethyl magnesium bromide. The latter reaction goes smoothly when a mixture of ether and benzene is used as solvent and leads to 1,2-dimethyl-3-(2'-penten-3'-yl)-5-methoxyindole (VIII).

EXPERIMENTAL

Ethyl ester of N-(o-tolyl)-β-aminocrotonic acid. 26 g of ethyl acetoacetate was mixed with 21.5 g of o-toluidine. 2 drops of concentrated hydrochloric acid were added to the resultant solution which was then stood overnight in the cold. Ether was added to the emulsified liquid, the ether layer was dried with sodium sulfate, and the ether was distilled off to leave an oil which was distilled at reduced pressure. Yield of ester 33 g.

B.p. 136-138° (5 mm), $n^{20}D$ 1.5550, d^{20}_4 1.048, MR_D 67.17; calc. 67.24.

Found %: C 71.22, 71.43; H 7.86, 7.91. $C_{13}H_{17}O_2N$. Calculated %: C 71.20; H 7.82.

Ethyl ester of N-cyclohexyl-β-aminocrotonic acid. The reaction was carried out as in the preceding experiment, starting with 26 g of ethyl acetoacetate and 23 g of cyclohexylamine. Yield of ester 30.5 g.

B.p. 108-110° (2 mm), $n^{20}D$ 1.4879, d^{20}_4 1.001, MR_D 60.81; calc. 61.02.

Found %: N 6.80, 6.95. $C_{12}H_{21}O_2N$. Calculated %: N 6.63.

Ethyl ester of 1-(o-tolyl)-2-methyl-5-hydroxyindole-3-carboxylic acid (I). To a solution of 5.4 g of p--benzoquinone in 15 ml of anhydrous acetone was added 17 g of ethyl N-(o-tolyl)-β-aminocrotonate with stirring and cooling. The mixture was heated for 1.5 hours on the water bath, and the resulting crystals of the indole (I) were filtered and washed with a little ether. The mother liquor was concentrated on the water bath to remove the acetone, and ether was added to the viscous oil. The resulting crystals were collected. After recrystallization from alcohol the yield of ethyl 1-(p-tolyl)-2-methyl-5-hydroxyindole-3-crotonate (I) was 4.2 g; m.p. 208-209°.

Found %: C 73.65; 73.68; H 6.35, 6.23. $C_{19}H_{19}O_3N$. Calculated %: C 73.76; H 6.19.

Ethyl ester of 1-cyclohexyl-2-methyl-5-hydroxyindole-3-carboxylic acid (II). The reaction was carried out as in the preceding experiment, starting with 5.4 g of p-benzoquinone, 16 g of ethyl N-cyclohexyl-β-amino-crotonate and 15 ml of acetone. The crystals of the indole were separated by addition of ether to the reaction liquid. Yield 5 g; m.p. 69°.

Found %: C 71.80, 71.79; H 7.74, 7.79. $C_{18}H_{23}O_3N$. Calculated %: C 71.73; H 7.69.

Ethyl ester of 2-methyl-5-hydroxy-6,7-dichloroindole-3-carboxylic acid (III). Solutions of 3 g of 2,3-dichloro-p-benzoquinone [6] in 15 ml of chloroform and 3.45 g of ethyl β-aminocrotonate [7] in 6 ml of chloroform were mixed at room temperature. Heat was generated. The mixture was heated for 1 hour on a water bath. The resulting crystals of the indole (III) (0.9 g) were collected. From the filtrate, which was left to evaporate at room temperature overnight, was obtained a further 1.2 g of indole (III). Yield 2.1 g, m.p. 237-238° (from aqueous dioxan).

Found %: C 50.09, 50.20; H 3.79, 3.84. $C_{12}H_{11}O_3NCl_2$. Calculated %: C 50.01; H 3.84.

Ethyl ester of 2-methyl-4,7-dichloro-5-hydroxyindole-3-carboxylic acid (IV). The reaction was carried out as in the preceding experiment, starting with 7.2 g of 2,5-dichloro-p-benzoquinone [6], 7.8 g of ethyl β--aminocrotonate [7] and 15 ml of chloroform. Yield of indole (IV) 5.3 g; m.p. above 320° (decomp.) after two recrystallizations from ether-chloroform mixture.

Found %: C 49.99, 50.17; H 3.75, 3.68. $C_{12}H_{11}O_3NCl_2$. Calculated %: C 50.01; H 3.84.

Ethyl ester of 1-ethyl-2-methyl-4,7-dichloro-5-hydroxyindole-3-carboxylic acid (V). A mixture of 7.2 g of 2,5-dichloro-p-benzoquinone [6], 9.35 g of ethyl N-ethyl-β-aminocrotonate [8], and 2 g of anhydrous ammonium chloride in 10 ml of anhydrous ethyl alcohol was heated for 1 hour on a water bath. The precipitate was separated, washed with water and dried at 120°. Yield of indole (V) 3.8 g; m.p. 247-248° (from alcohol-chloroform mixture).

Found %: C 53.15, 53.46; H 4.83, 4.80. $C_{14}H_{15}O_3NCl_2$. Calculated %: C 53.17; H 4.78.

Ethyl ester of 1-phenyl-2-methyl-5-hydroxybenzindole-3-carboxylic acid (VI). A solution of 3.2 g of α--naphthoquinone in 7.5 ml of anhydrous acetone was stirred (with cooling) with 6.1 g of ethyl N-phenyl-β-amino-crotonate [8], and the solution was heated for 1 hour on a water bath. The crystals of the benzindole (VI) were collected. The acetone was evaporated from the mother liquor and the residue treated with ether which brought down more crystals. Yield 1.7 g; m.p. 227° (from dioxan).

Found %: C 76.75, 76.80; H 5.68, 5.80; N 3.97, 4.02. $C_{22}H_{19}O_3N$. Calculated %: C 76.50; H 5.55; N 4.05.

Ethyl ester of 1,2-dimethyl-5-methoxyindole-3-carboxylic acid. To a solution of 17.1 g of ethyl 1,2-dimethyl-5-hydroxyindole-3-carboxylate [2] in 200 ml of dioxan was added 18.4 g of dimethyl sulfate, followed by 172 ml of 2 N sodium hydroxide. The mixture was shaken at room temperature for 6 hours. Dilution of the dioxan solution with water brought down the ethyl ester of 1,2-dimethyl-5-methoxyindole carboxylic acid. Yield 17.2 g, m.p. 114-115° (from methanol).

Found %: C 67.95, 68.05; H 7.04, 7.05. $C_{14}H_{17}O_3N$. Calculated %: C 67.99; H 6.93.

1,2-Dimethyl-5-methoxyindole-3-carboxylic acid. A solution of 2.9 g of the ethyl ester of 1,2-dimethyl--5-methoxyindole-3-carboxylic acid and 5.3 g of potassium hydroxide in 100 ml of ethyl alcohol were boiled for 5 hours; the alcohol was driven off and the dry residue dissolved in water. Acidification of the aqueous solution with hydrochloric acid (to Congo) gave 1,2-dimethyl-5-methoxyindole-3-carboxylic acid. Yield 1.95 g, m.p. 190-191° (from methanol).

Found %: C 65.82, 65.83; H 6.02, 6.09. $C_{12}H_{13}O_3N$. Calculated %: C 65.73; H 5.93.

1,2-Dimethyl-3-(penten-2'-yl-3')-5-methoxyindole (VII). A solution of 5 g of the ethyl ester of 1,2-dimethyl-5-methoxyindole-3-carboxylic acid in 150 ml of anhydrous benzene was gradually added to the organomagnesium compound prepared from 1.5 g of magnesium turnings and 5 g of ethyl bromide in 150 ml of absolute ether. The reaction mixture was heated for 4 hours at boiling point. After decomposition of the organomagnesium compound in the usual manner and removal of the solvent, the 1,2-dimethyl-3-(penten-2'-yl-3')-5-methoxyindole (VII) was distilled at reduced pressure. Yield 3 g, b.p. 163-165° (6 mm), m.p. 52-53° (from methanol).

Found %: C 78.94, 79.11; H 8.63, 8.56. $C_{16}H_{21}ON$. Calculated %: C 78.97; H 8.70.

Compound (VII) differs from the starting compound in easily decolorizing an ethereal solution of bromine.

1-Phenyl-2-methyl-3-acetyl-5-methoxyindole. The reaction was performed under the conditions of preparation of the ethyl ester of 1,2-dimethyl-5-methoxyindole-3-carboxylic acid, using 30 g of 1-phenyl-2-methyl--3-acetyl-5-hydroxyindole [3], 27.4 g of dimethyl sulfate, 240 ml of 2 N sodium hydroxide and 25 ml of dioxan. Yield of 1-phenyl-2-methyl-3-acetyl-5-methoxyindole 27.4 g ,m.p. 124-125° (from methanol).

Found %: C 77.35, 77.44; H 6.09, 5.99. $C_{18}H_{17}O_2N$. Calculated %: C 77.39; H 6.13.

Acidification of the aqueous alkaline solution led to separation of 3.1 g of unchanged starting compound.

Ethyl ester of 2-methyl-5-methoxy-6,7-dichloroindole-3-carboxylic acid. The reaction was performed under the conditions of the preceding experiment, starting with 0.6 g of ethyl ester of 2-methyl-5-hydroxy-6,7--dichloroindole-3-carboxylic acid (III), 0.5 ml of dimethyl sulfate, 10 ml of 2 N sodium hydroxide and 3 ml of dioxan. Yield of ethyl ester of 2-methyl-5-methoxy-6,7-dichloroindole-3-carboxylic acid 0.58 g, m.p. 133° (from aqueous dioxan)

Found %: C 51.62, 51.48; H 4.32, 4.39. $C_{13}H_{13}O_3NCl_2$. Calculated %: C 51.67; H 4.33.

Ethyl ester of 2-methyl-5-benzoxyindole-3-carboxylic acid.* 2.2 g of the ethyl ester of 2-methyl-5-hydroxyindole-3-carboxylic acid [2] was dissolved in 6 ml of pyridine. To the cooled solution was added 1.1 ml of benzoyl chloride and the reaction mixture was stood for 4 hours at room temperature. 100 ml of water was then added and the precipitate was collected and washed on the filter with 10% sulfuric acid (until the odor of pyridine had disappeared). The ethyl ester of 2-methyl-5-benzoxyindole-3-carboxylic acid was dried and recrystallized from alcohol. Yield 2.8 g, m.p. 175°.

Found %: C 70.33, 70.45; H 5.45, 5.47. $C_{19}H_{17}O_4N$. Calculated %: C 70.57; H 5.30.

Ethyl ester of 1-phenyl-2-methyl-5-benzoxyindole-3-carboxylic acid. The experiment was performed with 3 g of ethyl ester of 1-phenyl-2-methyl-5-hydroxyindole-3-carboxylic acid, 1.2 ml of benzoyl chloride and 9 ml of pyridine. Yield of ethyl ester of 1-phenyl-2-methyl-5-benzoxyindole-3-carboxylic acid 3.84 g, m.p. 120--121° (from dioxan).

Found %: C 75.15, 75.37; H 5.55, 5.62. $C_{25}H_{21}O_4N$. Calculated %: C 75.17; H 5.30.

Ethyl ester of 1-phenyl-2-methyl-5-benzoxybenzindole-3-carboxylic acid. The experiment was performed with 1.1 g of the ethyl ester of 1-phenyl-2-methyl-5-hydroxybenzindole-3-carboxylic acid (VI), 0.4 ml of benzoyl chloride and 3 ml of pyridine. Yield of ethyl ester of 1-phenyl-2-methyl-5-benzoxybenzidole-3-carboxylic acid 1.3 g, m.p. 185° (from alcohol-dioxane mixture).

* The benzoylation of other hydroxyindoles was effected by the procedure described in this experiment.

Found %: C 77.55, 77.42; H 5.36, 5.32. $C_{29}H_{23}O_4N$. Calculated %: C 77.48; H 5.16.

Ethyl ester of 1-(o-tolyl)-2-methyl-5-benzoxyindole-3-carboxylic acid. Reaction components were 3.2 g of the ethyl ester of 1-(o-tolyl)-2-methyl-5-hydroxyindole-3-carboxylic acid (I), 1.2 ml of benzoyl chloride and 6 ml of pyridine. Yield of benzoyl derivative 2.44 g; m.p. 146-147° (from alcohol).

Found %: N 3.40, 3.44. $C_{26}H_{23}O_4N$. Calculated %: N 3.39.

Ethyl ester of 1-(o-tolyl)-2-methyl-5-(3,5-dinitrobenzoxy)-indole-3-carboxylic acid. Reaction components were 3.2 g of the ethyl ester of 1-(o-tolyl)-2-methyl-5-hydroxyindole-3-carboxylic acid (I), 2.3 g of dinitrobenzoyl chloride and 9 ml of pyridine. Yield of benzoyl derivative 2.5 g, m.p. 121° (from alcohol-dioxan mixture).

Found %: C 62.18, 62.13; H 4.36, 4.32. $C_{26}H_{21}O_8N_3$. Calculated %: C 62.02; H 4.20.

Ethyl ester of 1-(o-tolyl)-2-methyl-5-(o-methoxybenzoxy)-indole-3-carboxylic acid. The experiment was performed with 2.9 g of ethyl ester of 1-(o-tolyl)-2-methyl-5-hydroxyindole-3-carboxylic acid, 1.6 g of o--methoxybenzoyl chloride and 6 ml of pyridine. Yield of benzoyl derivative 2.8 g, m.p. 171° (from alcohol).

Found %: C 72.33, 72.47; H 5.63, 5.73. $C_{26}H_{25}O_5N$. Calculated %: C 72.37; H 5.84.

Ethyl ester of 1-propionitrile-2-methyl-5-benzoxyindole-3-carboxylic acid. The experiment was carried out with 1.1 g of ethyl ester of 1-propionitrile-2-methyl-5-hydroxyindole-3-carboxylic acid [4], 0.7 g of benzoyl chloride and 8 ml of pyridine. Yield of ethyl ester of 1-propionitrile-2-methyl-5-benzoxyindole-3-carboxylic acid 1.2 g, m.p. 165° (from alcohol).

Found %: C 70.24, 70.27; H 5.30, 5.47. $C_{22}H_{20}O_4N_2$. Calculated %: C 70.20; H 5.36.

Ethyl ester of 1-ethyl-2-methyl-5-benzoxyindole-3-carboxylic acid. Reactants were 2.5 g of the ethyl ester of 1-ethyl-2-methyl-5-hydroxyindole-3-carboxylic acid [4], 1.4 g of benzoyl chloride and 12 ml of pyridine. Yield of benzoyl derivative 3.2 g, m.p. 137°.

Found %: C 72.01, 71.87; H 6.24, 6.07. $C_{21}H_{21}O_4N$. Calculated %: C 71.78; H 6.02.

SUMMARY

1. Condensation of p-quinones with the ethyl ester of β-aminocrotonic acid and its analogs gave a series of substituted hydroxyindoles.

2. A procedure for methylation and benzoylation of hydroxyindoles was developed.

3. The reaction of the ethyl ester of 1,2-dimethyl-5-methoxyindole-3-carboxylic acid with ethyl magnesium bromide was studied.

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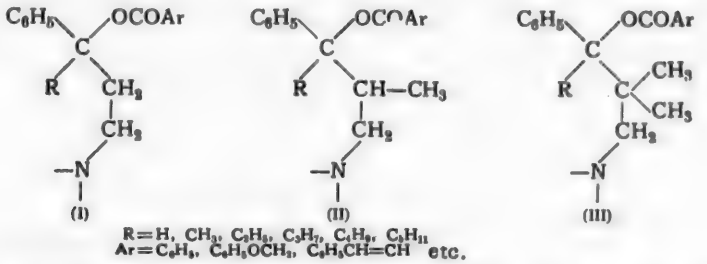
SYNTHETIC ANALGESICS

XXIV. ESTERS OF 1-PHENYL-2,2-DIMETHYL-3-DIALKYLAMINOPROPAN-1-OLS

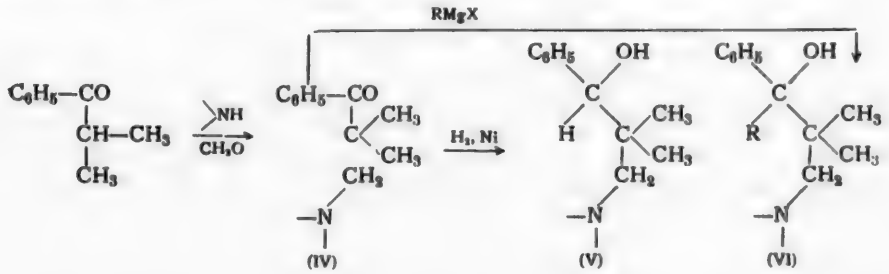
I. N. Nazarov, E. M. Cherkasova and Chan Chon Khvan

We have been engaged for some years in the search for new analgesics and anesthetics, and in preceding communications [1, 2] we described a series of esters of 1-phenyl-3-dialkylaminopropan-1-ols (I) and (II).

In the present paper we describe the synthesis of esters of 1-phenyl-2,2-dimethyl-3-dialkylaminopropan-1--ols (III). They were prepared with the objective of clarifying the effect of further branching of the dialkylaminopropane chain on the physiological activity of this type of complex ester.



Esters (III) were synthesized by a series of routes, previously developed by us, starting from isobutyrophenone. By the Mannich reaction the latter was converted to the aminoketones (IV) which were then hydrogenated to the corresponding secondary aminoalcohols (V). By the Grignard reaction, compounds (IV) were converted into the tertiary aminoalcohols (VI).



Secondary amines employed in the Mannich reaction were dimethylamine and piperidine. Treatment of the aminoalcohols (V) and (VI) with acid chlorides gave the corresponding esters (III), which were subjected to pharmacological examination in the form of the hydrochlorides, primarily with reference to their activity as surface anesthetics. The tests established that all* of the preparations possess high anesthetic activity. The most interesting compound

*With exception of one preparation (1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol p-nitrobenzoate) which was not tested due to its insolubility in water.

was found to be 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (No. 1 in table) whose activity was equal to that of dicaine but whose toxicity was very much lower. This preparation satisfactorily withstands sterilization in 0.5% solution. This ester surpasses dicaine in its ability to bring about conductive (radial) anesthesia. Investigation of the irritant action showed that this preparation in 1 and 2% solution resembles dicaine in not causing changes in the hypodermic tissue. Similar characteristics were exhibited by a number of other preparations (No. 2 to 5 in table). Consequently, the introduction of two methyl groups in the α,α-position to the carbon atom linked to hydroxyl favorably influences the pharmacological properties of the prepared esters of 1-phenyl-2,2-dimethyl-3-dialkylaminopropan-1-ols (III), especially in respect to stability during sterilization.

Results of the pharmacological tests (surface anesthesia) are shown in the Table.

Anesthetic Activity of Some Hydrochlorides of Esters (III) in Comparison with Dicaine

Preparation No.	Formula of preparation	Anesthetizing "index"			Anesthetizing index after sterilization (0.5%)	Mean lethal dose in mg/kg
		0.1%	0.25%	0.5%		
	Dicaine	683	1100	1300	1300	8.5
1	(III) R=C_2H_5, N=$N(CH_3)_2$, Ar=$C_6H_5OCH_2$	618	1294	1300	1300	19
2	(III) R=CH_3, N=$N(CH_3)_2$, Ar=$C_6H_5OCH_2CH_2$	44	314	1300	1300	24
3	(III) R=CH_3, N=$N(CH_3)_2$, Ar=C_6H_5	195	908	1300	1300	31
4	(III) R=CH_3, N=$N(CH_3)_2$, Ar=$C_6H_5CH=CH$	587	951	1300	1300	13.5
5	(III) R=CH_3, N=$N(CH_3)_2$, Ar=$C_6H_5OCH_2$	337	997	1300	1276	23.5

EXPERIMENTAL

The starting isobutyrophenone was synthesized by the Friedel-Crafts reaction in 81% yield from isobutyryl chloride (prepared from isobutyric acid and thionyl chloride) and benzene in presence of aluminum chloride [3].

β-Dimethylamino-α,α-dimethylpropiophenone (IV, N=$N(CH_3)_2$). 14.8 g of isobutyrophenone [3], 72 g of 25% aqueous dimethylamine and 35 g of 30% formalin were refluxed for 3 hours on a boiling water bath. The reaction mass was acidified with hydrochloric acid and extracted with ether for removalof neutral products. The hydrochloric acid solution was saturated with sodium carbonate; the product was extracted with ether, dried with sodium sulfate, and fractionally distilled in vacuo to give 3.1 g of β-dimethylamino-α,α-dimethylpropiophenone with b.p. 95-98° (3 mm).

Found %: C 76.78, 76.13; H 9.15, 8.97; N 6.92, 7.14. $C_{13}H_{19}ON$. Calculated %: C 76.30; H 9.26; N 6.82.

The hydrochloride of the aminoketone melted at 138-140° [7].

Found %: N 6.03. $C_{13}H_{19}ON \cdot HCl$. Calculated %: N 5.83.

1-Phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (V). 2.5 g of the aminoketone (IV, N=$N(CH_3)_2$)

in 50 ml of anhydrous alcohol was hydrogenated in presence of 3 g of Ni catalyst for 2 hours. The volume of hydrogen absorbed was 275 ml compared with the theoretical requirement of 250 ml. The catalyst was filtered off, the alcohol was driven off, and the residue was distilled in vacuo to give 1.68 g (81%) of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with b.p. 109-110° (3 mm) [4].

Found %: C 75.2, 75.57; H 10.41, 10.21; N 7.20, 6.88. $C_{13}H_{21}ON$. Calculated %: C 75.20; H 10.12; N 6.76.

The hydrochloride of the aminoalcohol melted at 174-175° (from acetone and alcohol).

Found %: N 5.42, 5.42. $C_{13}H_{21}ON \cdot HCl$. Calculated %: N 5.77.

1,2,2-Trimethyl-1-phenyl-3-dimethylaminopropan-1-ol [VI, $R = CH_3$, $N< = N(CH_3)_2$]. An ethereal solution of methyl magnesium iodide was prepared from 3.64 g of magnesium, 29 g of methyl iodide and 57 ml of anhydrous ether. 15.5 g of β-dimethylamino-α,α-dimethylpropiophenone (IV, $N< = N<^{CH_3}_{CH_3}$). was gradually stirred into the solution at 0-5°. The mixture was stirred for 2 hours at room temperature and left overnight. The next day it was stirred on a water bath at the boiling point of ether for about 2 hours. After cooling, the reaction mass was treated with saturated ammonium chloride solution, the neutral products were twice extracted with ether, and the acid layer was saturated with sodium carbonate. The resulting oil was repeatedly extracted with ether and dried with sodium sulfate. Yield 11.95 g (71.5%) of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan--1-ol with b.p. 103-104° (2 mm).

Found %: C 76.23, 76.31; H 9.74, 10.47; N 6.22, 6.21. $C_{14}H_{23}ON$. Calculated %: C 76.20; H 10.2; N 6.32.

The hydrochloride of the aminoalcohol melted at 85-86° (from acetone).

Found %: N 5.34. $C_{14}H_{23}ON \cdot HCl$. Calculated %: N 5.42.

1-Ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (VI, $R = C_2H_5$, $N< = N<^{CH_3}_{CH_3}$).

To a solution of ethyl magnesium bromide, prepared from 1.41 g of magnesium, 6.5 g of ethyl bromide and 22 ml of anhydrous ether, was gradually added dropwise with stirring at 0-5° 6.04 g of the aminoketone [IV, $N< = N(CH_3)_2$]. The product was worked up as described above. Yield 5.2 g (75%) of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with b.p. 118-119° (3mm).

Found %: C 76.31, 76.89; H 10.75, 11.01; N 5.55, 5.79. $C_{15}H_{25}ON$. Calculated %: C 76.6; H 10.62; N 5.92.

The hydrochloride of the aminoalcohol melted at 224-225°.

Found %: C 66.34, 66.75; H 9.51, 9.27; N 5.31. $C_{15}H_{25}ON \cdot HCl$. Calculted %: C 66.31; H 9.58; N 5.18.

α,α-Dimethyl-β-piperidylpropiophenone (IV, $N< = N<\bigcirc>$). 44.4 g of isobutyrophenone, 36.4 g of piperidine hydrochloride, 12 g of paraformaldehyde, 300 ml of dioxan and 0.5 ml of hydrochloric acid were heated on a boiling water bath until the paraformaldehyde had completely dissolved. The material was worked up in the usual manner to give 20.3 g (27.6%) of α,α-dimethyl-β-piperidylpropiophenone with b.p. 122-125° (2 mm); the hydrochloride had m.p. 157-158° (from acetone) (this aminoketone was obtained in a yield of 4% [5]).

1-Phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol [6] (V, $N< = N<\bigcirc>$). 9.8 g of α,α-dimethyl--β-piperidylpropiophenone in 100 ml of alcohol was hydrogenated in presence of nickel catalyst (prepared from

11 g of 75% alloy) with continuous shaking for 8 hours. 1060 ml of hydrogen was absorbed instead of 966 ml required by theory. The catalyst was filtered off, the alcohol was driven off, and the residue was acidified. The neutral products were extracted with ether and the aqueous acidic layer was treated with caustic alkali and repeatedly extracted with ether. After drying of the ether extract and removal of the ether, 9.8 g (99%) of 1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol was obtained with m.p. 74-75°.

Found %: N 6.03, 6.16. $C_{16}H_{25}ON$. Calculated %: N 5.70.

The hydrochloride melted at 223-224° (from acetone and alcohol).

Found %: N 5.37, 5.52. $C_{16}H_{25}ON \cdot HCl$. Calculated %: N 4.95.

1,2,2-Trimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (VI, $R = CH_3$, $N\langle = N\langle\rangle\rangle$). 11.14 g of α,α-dimethyl-β-piperidylpropiophenone in 20 ml of ether was gradually stirred at −10° into an ethereal solution of methyl magnesium iodide prepared from 3.8 g of magnesium, 20.2 g of methyl iodide and 60 ml of anhydrous ether. The next day the reaction mass was acidified, the neutral products were separated by extraction with ether, and the aqueous acid layer was treated with 20% alkali solution and repeatedly extracted with ether. After drying and removal of the ether, the product was fractionally distilled in vacuo to give 6.25 g (53%) of 1,2,2-trimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol with b.p. 120-124° (2 mm).

Found %: N 5.31, 5.19. $C_{17}H_{27}ON$. Calculated %: N 5.35.

The hydrochloride melts at 195-196° (from acetone and alcohol).

Found %: N 4.72, 4.88. $C_{17}H_{27}ON \cdot HCl$. Calculated %: N 4.73.

1-Ethyl-1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol (VI, $R = C_2H_5$, $N\langle = N\langle\rangle\rangle$). 24.5 g of α,α-dimethyl-β-piperidylpropiophenone was added under the above conditions to an ethereal solution of ethyl magnesium bromide prepared from 7.2 g of magnesium, 36.3 g of ethyl bromide and 50 ml of ether. The material was worked up as in the preceding experiment to give 23.4 g (85%) of 1-ethyl-1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol with m.p. 57-58°.

Found %: N 5.06, 5.31. $C_{18}H_{29}ON$. Calculated %: N 5.09.

The hydrochloride melted at 221-222° (from alcohol-acetone mixture).

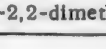
Found %: N 4.47, 4.64. $C_{18}H_{29}ON \cdot HCl$. Calculated %: N 4.48.

Phenoxyacetate of 1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol (III, $R = H$, $N\langle = N\langle\rangle\rangle$, $Ar = CH_2OC_6H_5$). 5 g of phenoxyacetyl chloride in 30 ml of chloroform was added at −10° to a solution of 4.94 g of 1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol in 30 ml of chloroform in presence of 0.1 g of magnesium. The following day the chloroform was distilled off. The residue was twice washed with ether, the ether was poured off and a fresh portion of ether was added. The precipitate was boiled for 30 minutes and recrystallized from a mixture of chloroform and acetone. Yield 4.94 g (59.2%) of the hydrochloride of the phenoxyacetate of 1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol with m.p. 193-194°.

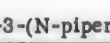
Found %: C 69.33, 69.42; H 7.18, 7.37; N 3.55, 3.65. $C_{24}H_{31}O_3N \cdot HCl$. Calculated %: C 69; H 7.69; N 3.36.

Phenoxyacetate of 1,2,2-trimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (III, $R = CH_3$, $N\langle = N\langle\rangle\rangle$, $Ar = CH_2OC_6H_5$). Reactants were 5.22 g of 1,2,2-trimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol, 0.1 g of magnesium, 5 g of phenoxyacetyl chloride in 30 ml of chloroform. The mixture was heated for 2 hours on a water bath at 50-60°. The following day the solvent was driven off in a low vacuum and the oily residue dissolved in 50 ml of anhydrous acetone and a little ether. 7.56 g of technical product with m.p. 80-84° was isolated. It was recrystallized from chloroform to give 5.12 g (59.5%) of the hydrochloride of the phenoxyacetate of 1,2,2-trimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol with m.p. 94-95°.

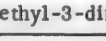
Found %: N 3.50, 3.57. $C_{25}H_{33}O_3N \cdot HCl$. Calculated %: N 3.24.

Phenoxyacetate of 1-ethyl-1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol (III, R = C_2H_5, N = N  , Ar = $CH_2OC_6H_5$). A mixture of 5.51 g of 1-ethyl-1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol, 3.6 g of phenoxyacetyl chloride, 0.1 g of magnesium and 60 ml of chloroform was heated for 2 hours on a water bath, after which dry hydrogen chloride was passed through the solution. The solvent was driven off in a low vacuum, and the residue was dissolved in a 1 : 1 mixture of chloroform and acetone. Cooling brought down the hydrochloride of the original aminoalcohol which did not show a depression of melting point in admixture with an authentic specimen. Ether was added to the mother liquor until the thick oil had completely separated; the latter was dried in a vacuum-desiccator for 40-50 hours using a powerful water jet pump. A cotton wool-like precipitate of the hydrochloride of the phenoxyacetate of 1-ethyl-1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol was formed; yield 1.95 g (21.9%); m.p. 135-138° (from acetone).

Found %: C 69.90, 70.10; H 8.03, 8.19; N 3.32, 3.33, $C_{26}H_{35}O_3N \cdot HCl$. Calculated %: C 69.9; H 8.1; N 3.14.

Benzoate of 2,2-dimethyl-1-phenyl-3-(N-piperidyl)-propan-1-ol (III, R = H, N  , Ar = C_6H_5). A mixture of 4.95 g of 1-phenyl-2,2-dimethyl-3-(N-piperidyl)propan-1-ol, 4.22 g of benzoyl chloride, 0.1 g of magnesium and 50 ml of chloroform was kept at room temperature for 24 hours and then heated for 1 hour at 50-60°. The magnesium granules were separated, the solvent was distilled off, and the residue was recrystallized from a 3 : 1 acetone-chloroform mixture. Yield 6.29 g (81.3%) of the hydrochloride of the benzoate of 1-phenyl-2,2-dimethyl-3-(N-piperidyl)-propan-1-ol with m.p. 193-195°.

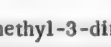
Found %: C 71.71, 71.57; H 7.98, 7.69; N 3.68, 3.51. $C_{23}H_{29}O_2N \cdot HCl$. Calculated %: C 71.40; H 7.75; N 3.62.

Cinnamic ester of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (III, R = H, N  , Ar = $C_6H_5CH{=}CH$). A mixture of 2.07 g of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol, 5 ml of anhydrous benzene, 3.3 g of cinnamyl chloride and 0.1 g of magnesium was heated for 1.5 hours on a boiling water bath. The next day the solvent was distilled off in vacuo, and the residue was dissolved in water and acidified with hydrochloric acid. The neutral products were extracted with ether several times. The aqueous layer was treated with sodium carbonate, the liberated base was extracted with ether, dried with sodium sulfate and fractionally distilled in vacuo to give 1.2 g (35.5%) of the cinnamic ester of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with b.p. 180° (2 mm), m.p. 85-86°.

Found %: C 78.92, 79.55; H 7.74, 7.82; N 4.40, 4.47. $C_{22}H_{27}O_2N$. Calculated %: C 78.50; H 7.98; N 4.17.

The hydrochloride melted at 129-130° (from acetone).

Found %: N 3.39, 3.32. $C_{22}H_{27}O_2N \cdot HCl$. Calculated %: N 3.74.

Phenoxyacetate of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (III, R=H, N  , Ar = $CH_2OC_6H_5$). 3.41 g of phenoxyacetyl chloride in 5 ml of benzene was gradually run with cooling into a solution of 2.07 g of 1-phenyl-2,2-dimethylaminopropan-1-ol in 5 ml of anhydrous benzene. Heating and crystallization of the whole mass were observed. Anhydrous ether was added and the mixture heated for 2 hours at the boiling point of ether. The latter was run off; the solid was washed several times with ether and twice recrystallized from chloroform to give 2 g (54%) of the hydrochloride of the phenoxyacetate of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with m.p. 210-211°.

Found %: C 67.02, 66.50; H 7.14, 7.48; N 3.71, 3.76. $C_{21}H_{27}O_3N \cdot HCl$. Calculated %: C 66.80; H 7.41; N 3.71.

Benzoate of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (III, R = H, $N\langle = N\langle^{CH_3}_{CH_3}$, Ar = C_6H_5). Under the conditions of the preceding experiment, 2.07 g of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol and 2.81 g of benzoyl chloride were reacted to give 2.2 g (63%) of the hydrochloride of the benzoate of 1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with m.p. 201-202° (from acetone and alcohol).

Found %: C 68.97, 69.23; H 7.48, 7.23; N 3.87, 4.13. $C_{20}H_{25}O_2N \cdot HCl$. Calculated %: C 69.10; H 7.49; N 4.04.

Phenoxyacetate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol (III, R = CH_3, $N\langle = N\langle^{CH_3}_{CH_3}$, Ar = $CH_2OC_6H_5$). 2.35 g of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol and 5.45 g of phenoxyacetyl chloride in 10 ml of anhydrous benzene were kept for 12 hours at 0°. The material was then worked up as in the preceding experiment to give 2.2 g (59%) of the hydrochloride of the phenoxyacetate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol with m.p. 117-118° (from acetone).

Found %: C 67.84, 67.73; H 7.36, 7.84; N 3.34, 3.42. $C_{22}H_{29}O_3N \cdot HCl$. Calculated %: C 68.10; H 7.72; N 3.61.

Cinnamic ester of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol (III, R = CH_3, $N\langle = N\langle^{CH_3}_{CH_3}$, Ar = $C_6H_5CH{=}CH$). Under conditions similar to those described above, 2.21 g of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol and 3.33 g of cinnamyl chloride in 5 ml of anhydrous benzene gave 2.5 g (62%) of the hydrochloride of the cinnamate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol with m.p. 204-205°.

Found %: C 71.20, 71.32; H 7.78, 7.49; N 3.96, 3.92. $C_{23}H_{29}O_2N \cdot HCl$. Calculated %: C 71.20; H 7.74; N 3.62.

Benzoate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol (III, R = CH_3, $N\langle = N\langle^{CH_3}_{CH_3}$, Ar = C_6H_5). Reactants were 2.21 g of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-ol and 3 g of benzoyl chloride in 5 ml of anhydrous benzene. The reaction mass was worked up as in the preceding experiments to give 2.5 g (69%) of the hydrochloride of the benzoate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol with m.p. 202-205° (from chloroform and anhydrous alcohol).

Found %: C 69.48, 69.54; H 8.06, 8.03; N 4.10, 3.89. $C_{21}H_{27}O_2N \cdot HCl$. Calculated %: C 69.80; H 7.75; N 3.88.

p-Nitrobenzoate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol (III, R = CH_3, $N\langle = N\langle^{CH_3}_{CH_3}$, Ar = $C_6H_4NO_2$-p). 2.21 g of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol and 3.71 g of p-nitrobenzoyl chloride in 15 ml of anhydrous benzene, reacted under the above-described conditions, gave 3.35 g (84%) of the hydrochloride of the p-nitrobenzoate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol with m.p. 205-206° (from acetone and anhydrous alcohol).

Found %: C 62.53, 62.33; H 6.41; 6.89; N 6.99, 6.88. $C_{21}H_{26}O_4N_2 \cdot HCl$. Calculated %: C 62.00; H 6.14; N 6.90.

Phenoxypropionate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol (III, R = CH_3, $N\langle = N\langle^{CH_3}_{CH_3}$, Ar = $CH_2CH_2OC_6H_5$). 2.21 g of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol and 3.71 g of phenoxypropionyl chloride in 5 ml of anhydrous benzene were heated for 2 hours on a boiling water bath. Anhydrous ether was then added and the whole mass was triturated. The ether was run off, a fresh portion of ether was added, and the trituration was repeated until the oil-like slurry started to solidify, after which 5 ml of anhydrous acetone was added and the resultant precipitate was recrystallized from chloroform to give 0.5 g (12.5%) of the hydrochloride of the phenoxypropionate of 1,2,2-trimethyl-1-phenyl-3-dimethylaminopropan-1-ol with m.p. 174-175°

Found %: C 67.73, 67.84; H 7.67, 7.82; N 3.64, 3.77. $C_{23}H_{31}O_3N \cdot HCl$. Calculated %: C 68.00; H 7.88; N 3.46.

Cinnamic ester of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (III, $R = C_2H_5$, $N\langle = N\langle^{CH_3}_{CH_3}$, $Ar = C_6H_5CH{=}CH$). 3.33 g of cinnamyl chloride was added to 2.35 g of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol in 5 ml of anhydrous benzene. After 2-hours' heating on a boiling water bath, crystals began to come down. These were worked up with anhydrous ether to give 1.7 g (42.5%) of the hydrochloride of the cinnamate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with m.p. 186-186.5° (from anhydrous alcohol).

Found %: C 71.57, 71.65; H 7.75, 8.09; N 3.12, 3.40. $C_{24}H_{31}O_2N \cdot HCl$. Calculated %: C 71.80; H 7.98. N 3.48.

Phenoxyacetate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (III, $R = C_2H_5$, $N\langle = N\langle^{CH_3}_{CH_3}$, $Ar = CH_2OC_6H_5$). 2.35 g of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol and 3.41 g of phenoxyacetyl chloride in 5 ml of anhydrous benzene were reacted under the conditions of the preceding experiment to give 2.2 g (54.5%) of the hydrochloride of the phenoxyacetate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with m.p. 148-149° (from acetone).

Found %: C 67.96; H 7.63; N 3.35, 3.70. $C_{23}H_{31}O_3N \cdot HCl$. Calculated %: C 68.00; H 7.88; N 3.45.

Benzoate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (III, $R = C_2H_5$, $N\langle = N\langle^{CH_3}_{CH_3}$, $Ar = C_6H_5$). Under the above-described conditions, 2.35 g of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol and 2.81 g of benzoyl chloride in 8 ml of anhydrous benzene gave 1.8 g (48%) of the hydrochloride of the benzoate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with m.p. 168-169° (from anhydrous alcohol).

Found %: N 4.36, 4.21. $C_{22}H_{29}O_2N \cdot HCl$. Calculated %: N 3.74.

p-Nitrobenzoate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol (III, $R = C_2H_5$, $N\langle = N\langle^{CH_3}_{CH_3}$, $Ar = C_6H_4NO_2\text{-}p$) Reaction as above between 2.35 g of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol and 3.71 g of p-nitrobenzoyl chloride in 8 ml of anhydrous benzene gave 2.2 g (52.5%) of the hydrochloride of the p-nitrobenzoate of 1-ethyl-1-phenyl-2,2-dimethyl-3-dimethylaminopropan-1-ol with m.p. 176-177° (from chloroform).

Found %: C 62.67, 62. 46; H 6.75, 6.60; N 6.85, 6.75. $C_{22}H_{28}O_4N_2 \cdot HCl$. Calculated %: C 62.80; H 6.70; N 6.69.

SUMMARY

1. A series of esters of 1-phenyl-2,2-dimethyl-3-dialkylaminopropan-1-ols with a branched propanol chain was synthesized for the purpose of pharmacological tests. Aminoketones and aminoalcohols with dimethylamine and piperidine residues were also obtained as intermediate products.

2. Some of the synthesized compounds exhibited high anesthetic activity. The phenoxyacetate of 1-ethyl-2,2-dimethyl-1-phenyl-3-dimethylaminopropan-1-ol is equivalent to dicaine in anesthetizing activity but is considerably less toxic and is stable when sterilized in 0.5% solution.

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ACETYLENE DERIVATIVES

190. PREPARATION OF ETHOXYACETYLENE AND ITS EMPLOYMENT FOR THE SYNTHESIS OF UNSATURATED ALDEHYDES AND ACIDS

I. N. Nazarov, Zh. A. Krasnaia and V. P. Vinogradov

At the start of our investigations on the synthesis of polyenic compounds and isoprenoids, we considered the possibility of using ethoxyacetylene for this purpose.

Alkoxyacetylenes were first prepared by A. E. Favorskii and M. N. Shchukina [1] in 25% yield from vinyl ethers. Another method was developed by Jacobs [2] whereby β-bromovinylalkyl ethers are obtained from acetals of bromoacetaldehyde in 18% yield. Eglinton and coworkers described a new method of preparation of alkoxyacetylenes from haloacetals in one step by the action of sodium amide in liquid ammonia; yield 60% [3]. This method suffers, however, from a number of disadvantages associated with working with liquid ammonia, the very large consumption of sodium and the danger of explosion due to the exceptional sensitivity of the sodium derivative of ethoxyacetylene to the air.

The use of ethoxyacetylene has been limited in the past by its difficult accessibility due to the complexity of the methods of preparation.

We prepared ethoxyacetylene by a modification of the method of A. E. Favorskii and M. N. Shchukina, starting from vinyl ethyl ether. The latter was brominated in the absence of a solvent by adding it to cooled bromine [4]. This procedure excludes secondary reactions and leads to exhaustive bromination of vinyl ethyl ether. The so-prepared α,β-dibromodiethyl ether was used for preparation of β-bromovinyl ethyl ether without prior distillation. Considerable difficulties had attended the preparation of β-bromovinyl ethyl ether – the principal intermediate for production of ethoxyacetylene. A repetition of the literature method [1] of preparation of β-bromovinyl ethyl ether from α,β-dibromoethyl ether showed this method to be totally unsuitable for work with large quantities (300-400 g) since the heating of α,β-dibromoethyl ether with diethylaniline in a medium of anhydrous vaseline oil at 90-95° was accompanied by sudden rise of temperature to 160° with formation of resin and a small quantity of the acetal of bromoacetaldehyde.

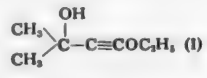
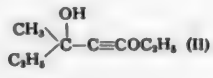
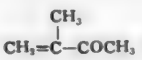
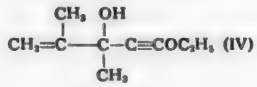
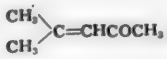
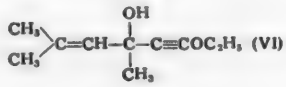
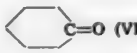
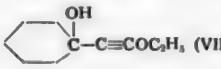
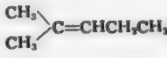
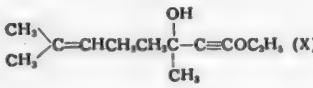
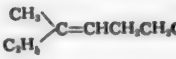
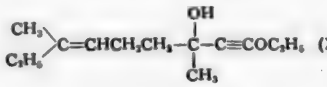
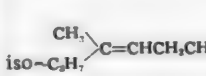
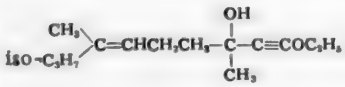
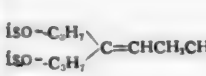
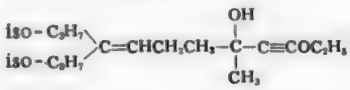
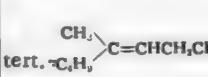
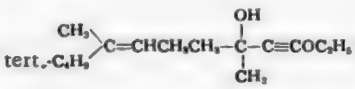
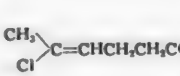
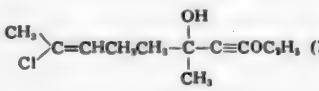
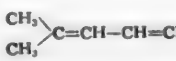
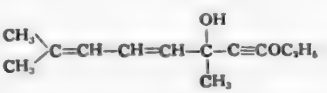
In a detailed investigation of this reaction we found that hydrogen bromide could be most conveniently split off from α,β-dibromodiethyl ether by gradual addition of the latter to diethylaniline in vacuo with simultaneous distillation of the resulting β-bromovinyl ethyl ether. The latter was obtained in 70-75% yield (on the original vinyl ethyl ether) in the form of a mixture of isomers, rectification of which in a column gave 17% of trans- and 83% of cis-isomer.

Ethoxyacetylene was prepared by subjecting β-bromovinyl ether (the mixture of isomers) to heating and mechanical stirring with pulverized potassium hydroxide in a vacuum of about 200 mm. The yield of pure ethoxyacetylene was 63% (on the β-bromovinyl ether taken). An increased yield in this step was difficult to obtain because the trans-isomer of β-bromovinyl ether was recovered unchanged.

Our new method thus enables the preparation of larger quantities of ethoxyacetylene in 44% yield (on the starting vinyl ethyl ether) whereas the literature method can only be operated with small quantities and the yield is only 25%.

It is well-known that ethoxyethynyl magnesium bromide readily enters into reaction with ketones to form

TABLE 1

No.	Starting ketones	Ethoxyethynyl carbinols	Yield (in %)
1		 (I)	77 *
2		 (II)	68.5 *
3	 (III)	 (IV)	55 *
4	 (V)	 (VI)	63 *
5	 (VII)	 (VIII)	76 *
6	 (IX)	 (X)	92
7	 (XI)	 (XII)	80
8	 (XIII)	 (XIV)	80
9	 (XV)	 (XVI)	70
10	 (XVII)	 (XVIII)	70
11	 (XIX)	 (XX)	61
12	 (XXI)	 (XXII)	63

* Yield based on the ethoxyacetylene taken into reaction; in the remaining cases the yield is calculated on the ketone.

ethoxyethynyl carbinols [5-7]. Addition of one molecule of hydrogen to ethoxyethynyl carbinols in presence of Pd catalyst gives ethoxyvinyl carbinols, which under the action of dilute acids are transformed into α,β-unsaturated aldehydes. Ethoxyethynyl carbinols in an acid medium are transformed into esters of α,β-unsaturated acids.

We studied the condensation of ethoxyacetylene with saturated, unsaturated and cyclic ketones. Ethoxyethynyl carbinols were synthesized by two routes; reaction of ketones with ethoxyethynyl magnesium bromide (the Iotsich reaction) and reaction of ketones with ethoxyacetylene in presence of potassium hydroxide (the Favorskii reaction).

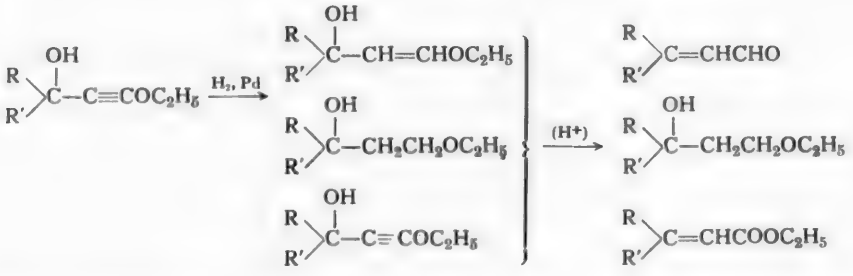
The ethoxyethynyl carbinols prepared by the first method are listed in Table 1 [all of the carbinols except (I) and (X) were synthesized for the first time]. The yield of ethoxyethynyl carbinols from saturated, cyclic and γ,δ-unsaturated ketones was 70-92%. This reaction goes the most smoothly with methylheptenone (XI) and its analogs (XI), (XIII), (XV) and (XVII). The yield of 2,6-dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X) (starting material for the synthesis of citral) was 92% as compared with the 73% reported in the literature [7].

Addition of ethoxyethynyl magnesium bromide to α,β-unsaturated ketones [methylisopropenyl ketone (III), mesityl oxide (V) and methylheptadienone (XXXI)] takes place normally in the 1,2-position with formation of the corresponding ethoxyethynyl carbinols (yield 55-63%).

Ethoxyethynyl carbinols had previously never been obtained by the Favorskii reaction. It was found that this method gives ethoxyethynyl carbinols in lower yields than when using ethoxyethynyl magnesium bromide. Thus, the yield of dimethylethoxyethynyl carbinol (I) by the Favorskii method was 39% (against 77%), and that of 2,6-dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X) was 58% (against 92%).

Ethoxyethynyl carbinols were hydrogenated in ethereal solution in presence of Pd catalyst to give ethoxyvinyl carbinols. In presence of 3% sulfuric or 5% oxalic acid, the latter (without distillation) are easily converted into α,β-unsaturated aldehydes (Table 2).

Hydrogenation of ethoxyethynyl carbinols in presence of Pd catalyst is not entirely selective. This is reflected in all cases in the separation of a secondary product boiling 10-15° higher than the corresponding aldehyde and having a lower refractive index. The experiment on preparation of citral, for example, gave a fraction with b.p. 75-79° (1.5 mm), $n^{21}D$ 1.4639, not possessing aldehydic properties. This fraction was exhaustively hydrogenated in presence of Pt catalyst; 1.5 moles of hydrogen per mole of compound were absorbed. The product of hydrogenation was a mixture of substances boiling at 65-73° (1.5 mm) whose empirical analysis corresponded to the formula $C_{12}H_{26}O_2$. The product of exhaustive hydrogenation is presumably a mixture of the ethyl ester of tetrahydrogeranic acid and 3,7-dimethyl-1-ethoxyoctan-3-ol. The secondary product with b.p. 75-79° (1.5 mm) formed during the preparation of citral is probably a mixture of fully hydrogenated ethoxyacetylenic carbinol and the ethyl ester of geranic acid. These secondary products are formed because the hydrogenation of the triple bond is not strictly selective.



The selectivity of hydrogenation of ethoxyacetylenic carbinols depends on their structure. Carbinols prepared from methylheptenone and its analogs are hydrogenated more selectively than carbinols synthesized from acetone, methyl ethyl ketone, cyclohexanone and other similar ketones; citral and its analogs are therefore obtained from ethoxyacetylenic carbinols in high yield (80-90%).

Hydrogenation of ethoxyacetylenic carbinols in presence of copper-nickel catalyst [13] is entirely unselective.

We observed that dialkylethoxyvinyl carbinols are converted to a considerable extent into α,β-unsaturated

aldehydes even in the absence of acid. For example, distillation of the product of partial hydrogenation of dimethylethoxyethynyl carbinol (I) gave dimethylacrolein (XXIII) in 59% yield. This is accounted for by the facility of allylic rearrangement of ethoxyvinyl carbinols to form half acetals which are transformed into α,β-unsaturated aldehydes.

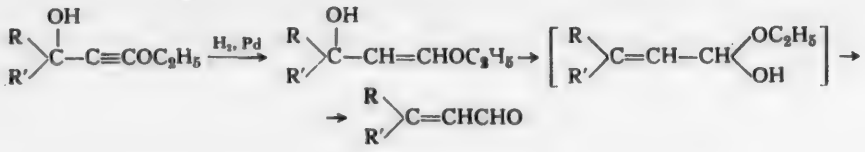
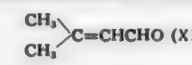
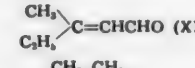
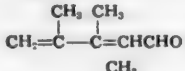
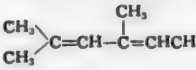
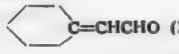
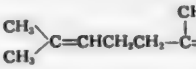
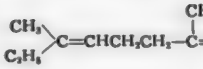
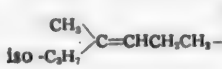
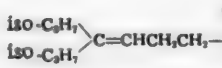
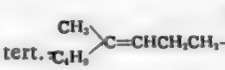
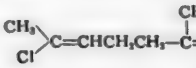
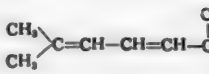


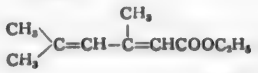
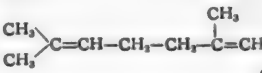
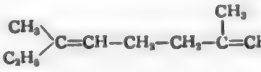
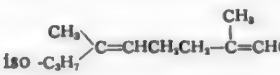
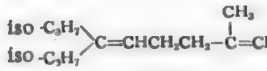
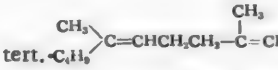
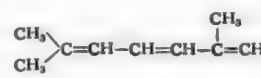
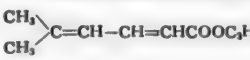
TABLE 2

Prep. No.	Aldehydes	Yield of aldehydes (in %)
1	 (XXIII)	74
2	 (XXIV)	66
3	 (XXV)	60
4	 (XXVI)	40
5	 (XXVII)	52
6	 (XXVIII)	83
7	 (XXIX)	91.6
8	 (XXX)	81
9	 (XXXI)	86
10	 (XXXII)	75
11	 (XXXIII)	84
12	 (XXXIV)	40 *

*Yield based on the methylheptadienone; in the remaining cases on the ethoxyacetylenic carbinol.

Ethoxyacetylenic carbinols are converted into ethyl esters of α,β-unsaturated acids (Table 3) in high yield under the action of 10% sulfuric acid at room temperature. Some of the prepared esters were hydrolyzed by a methanol solution of potassium hydroxide to form the corresponding α,β-unsaturated acids. In none of the numerous experiments on conversion of ethoxyacetylenic carbinols into α, β-unsaturated aldehydes and esters did we obtain β-hydroxy compounds [6].

TABLE 3

Prep. No.	Esters of acids	Yield of esters (in %)
1	(XXXV)	65.5 *
2	(XXXVI)	87
3	 (XXXVII)	62.5
4	 (XXXVIII)	90
5	 (XXXIX)	89
6	 (XL)	90
7	 (XLI)	80
8	 (XLII)	85
9	(XLIII)	82.5
10	 (XLIV)	34 *
11	$C_6H_5CH{=}CHCOOC_2H_5$ (XLV)	50 *
12	$C_5H_7CH{=}CHCOOC_2H_5$ (XLVI)	51 *
13	 (XLVII)	28.3*

* The ethoxyacetylenic carbinol was not isolated in the pure form and the yield is therefore based on the ketone or aldehyde; in the remaining cases the yield is based on the ethyoxyethynyl carbinol.

The literature is lacking in any information about the manner of reaction of ethoxyethynyl magnesium bromide with aldehydes.** We studied the reaction of ethoxyethynyl magnesium bromide with acetaldehyde,

** After the present paper had been completed and had gone to press, a paper was published on the reaction of aldehydes with ethoxyethynyl magnesium bromide [14].

n-butyraldehyde, dimethylacrolein and benzaldehyde. It was found that the secondary ethoxyethynyl carbinols prepared from the aldehydes are extremely unstable. Attempts to distill these substances in vacuo in a nitrogen stream led in some cases (acetaldehyde, dimethylacrolein) even at room temperature to spontaneous decomposition accompanied by intense heat liberation and formation of resin. The formation of ethoxyethynyl carbinols from aldehydes and ethoxyacetylene is nevertheless confirmed by the fact that shaking of the ethereal extracts of these carbinols, obtained after reaction, with 10% sulfuric acid resulted in separation in yields of up to 50% of the corresponding ethyl esters of α,β-unsaturated acids [Table 3, compounds (XLV)-(XLVII)].

EXPERIMENTAL

1. Bromination of vinyl ethyl ether. 450 g (6.25 moles) of dry, distilled vinyl ethyl ether was gradually added, with stirring and cooling to −5°, to 1000 g (6.25 moles) of bromine (pure for analysis). 1450 g of α,β-dibromodiethyl ether was obtained and was used without distillation for preparation of β-bromovinyl ethyl ether.

2. Cleavage of hydrogen bromide from α,β-dibromodiethyl ether. 2300 g of dry diethylaniline (15.4 moles) was placed in a 4-liter, 3-necked flask fitted with stirrer (vacuum seal), dropping funnel and Vigreux column (the latter connected to a sloping condenser). A vacuum of 13-15 mm was created in the system, and the diethylaniline was heated to 90-95°. Addition of 1450 g (6.25 moles) of α,β-dibromodiethyl ether was made in the course of 4 hours to the heated diethylaniline. Within a few minutes after the start of addition of the dibromo ether, β-bromovinyl ethyl ether began to distil off in admixture with a little diethylaniline. The distillate was collected in an ice-cooled receiver. Fractionation of the distillate gave 655 g (70%) of β-bromovinyl ethyl ether with b.p. 42-46° (12 mm), $n^{20}D$ 1.4700. Fractionation of 50 g of β-bromovinyl ethyl ether in an 18-plate column gave the following fractions:

a) 7.0 g (17%) of trans-isomer.

B.p. 39-40° (28 mm), $n^{20}D$ 1.4648, d^{20}_4 1.4120, MR 29.54; calc. 29.61; μ 2.36 D.*

Found %: C 31.99, 32.11; H 4.70, 4.66. C_4H_7OBr. Calculated %: C 31.81; H 4.67.

b) 34.8 g (83%) of cis-isomer.

B.p. 51-51.8° (28 mm), $n^{20}D$ 1.4750. d^{20}_4 1.4310, MR 29.63; calc. 29.61; μ 2.8.

Found %: C 31.79, 31.74; H 4.50, 4.63. C_4H_7OBr. Calculated %: C 31.81; H 4.67.

Cleavage of hydrogen bromide from β-bromovinyl ethyl ether. Ethoxyacetylene. 600 g (4 moles) of β-bromovinyl ethyl ether (mixture of isomers) and 1200 g (21.4 moles) of powdered potassium hydroxide were put into a three-necked flask. A vacuum of 180-200 mm was established in the system and the reaction mass was mechanically stirred and heated on an oil bath. At a bath temperature of 95-105° the ethoxyacetylene rapidly distilled into a receiver cooled with solid carbon dioxide. The product was dried with potassium carbonate and distilled to give 175 g (63%) of ethoxyacetylene with b.p. 22-25° (180 mm), $n^{20}D$ 1.3800 [1].

In this experiment 115 g of unreacted trans-isomer of β-bromovinyl ethyl ether was obtained (b.p. 45-47° at 28 mm, $n^{20}D$ 1.4625), from which hydrogen bromide could not be split off on treatment for a second time with potassium hydroxide.

Dimethylethoxyethynyl carbinol (I). To the ethyl magnesium bromide prepared from 9.7 g of magnesium and 47 g (0.43 mole) of ethyl bromide in 140 ml of absolute ether was gradually added (while stirring) 29.4 g (0.42 mole) of freshly distilled ethoxyacetylene in 60 ml of absolute ether. When the addition was completed, the reaction mass was heated for 15 minutes at 35° until ethane ceased to come off, after which 26 g (0.45 mole) of acetone in 25 ml of absolute ether was gradually added while being cooled with a freezing mixture. The mixture was stirred for 30 minutes at room temperature and for 15 minutes at 35°; it was then cooled with ice and treated with 20% ammonium chloride solution. The ethereal layer was separated and the aqueous layer was extracted with three portions of ether. The combined ethereal extracts were dried with calcined potassium carbonate. Distillation gave 40.2 g (77%) of dimethylethoxyethynyl carbinol (I) with b.p. 67-68° (9 mm), $n^{20}D$ 1.4428, in agreement with the literature data [6].

b) 16.8 g (0.3 mole) of pulverized potassium hydroxide and 80 ml of absolute ether were placed in a three-necked flask fitted with mechanical stirrer, dropping funnel and condenser. In the course of 45 minutes, with iced-water cooling and vigorous stirring, a mixture of 10.5 g (0.15 mole) of ethoxyacetylene and 8.7 g (0.15 mole)

* Dipole moments were determined in benzene solution at 25° by the beat method in the department of physical chemistry of our institute.

of acetone in 25 ml of absolute ether was added. The reaction mass was stirred for 45 minutes at 0° and for 3 hours at room temperature. Addition was then made, with iced-water cooling, of 35 ml of water; the ethereal layer was separated and the aqueous layer was extracted with ether. The ethereal extract was saturated with carbon dioxide and dried with potassium carbonate. Distillation in vacuo gave 7 g of dimethylethoxyethynyl carbinol (I) with b.p. 65-66° (11 mm).

β,β-Dimethylacrolein (XXIII). a) 15 g of freshly distilled dimethylethoxyethynyl carbinol (I) in 30 ml of absolute ether was hydrogenated in presence of 5% palladium deposited on calcium carbonate with cold-water cooling. After 1.5 hours 1 mole of hydrogen (2,842 ml, 758 mm, 22°) had been absorbed, and hydrogenation was stopped. After separation of the catalyst, the bright-red solution was evaporated and distilled to give the following fractions: 1st, 132-135° (760 mm), $n^{19}D$ 1.4523, 5.8 g; 2nd, 55-59° (13 mm), $n^{19}D$ 1.4261, 2.3 g.

The first fraction was β,β-dimethylacrolein (XXIII), the 2,4-dinitrophenylhydrazone of which melted at 179-180° [9] (from ethyl alcohol-ethyl acetate mixture); λ^{*}_{max} (in isooctane) 350, 366, 380 mμ.

b) 15.45 g of freshly distilled dimethylethoxyethynyl carbinol (I) in 30 ml of absolute ether was hydrogenated in presence of Pd catalyst (cooling with water). The calculated quantity of hydrogen (2,890 ml; 763 mm, 20°) was absorbed after 1.5 hours, and hydrogenation was stopped. After the catalyst had been separated, 5 ml of 3% sulfuric acid was added to the ethereal solution, and the mixture was shaken for 45 minutes. The ethereal layer was washed with 10 ml of 5% sodium bicarbonate solution and 10 ml of water, and dried with calcined magnesium sulfate.

Distillation gave 7.5 g of β,β-dimethylacrolein (XXIII) with b.p. 133-135° (760 mm), $n^{19}D$ 1.4520, and 1 g of higher boiling fraction with b.p. 48-54° (10 mm), $n^{19}D$ 1.4255.

Methylethylethoxyethynyl carbinol (II). To the ethyl magnesium bromide prepared from 6.7 g of magnesium and 30.5 g (0.28 mole) of ethyl bromide in 100 ml of absolute ether was gradually added, with stirring, 20 g (0.286 mole) of freshly distilled ethoxyacetylene. The reaction mass was heated for 15 minutes at 35° until ethane ceased to be evolved, after which 22.2 g (0.308 mole) of methyl ethyl ketone and 25 ml of ether were added to the cooled mixture. The latter was stirred for 30 minutes at room temperature, and for 45 minutes at 35°; it was then cooled with ice and treated with 20% ammonium chloride solution. The ethereal layer was separated and the aqueous layer was extracted several times with ether. The combined ethereal extracts were dried with calcined magnesium sulfate and distilled to give 27.8 g of methylethylethoxyethynyl carbinol (II).

B.p. 73-74° (8 mm), $n^{20}D$ 1.4470, d^{20}_4 0.9357, MR 40.55; calc. 40.25.

Found %: C 67.29, 67.22; H 9.88, 10.10. $C_8H_{14}O_2$. Calculated %: C 67.60; H 9.88.

Ethyl ester of β-methyl-β-ethylacrylic acid (XXXVI). 10 g of methylethylethoxyethynyl carbinol (II) was shaken for 5 minutes with 100 ml of 10% sulfuric acid. The temperature of the reaction mass rose to 43°. The organic layer was collected and the aqueous layer extracted several times with ether. The ethereal solution was washed with water until neutral and dried; the ether was driven off and the residue distilled in vacuo to give 8.7 g of the ethyl ester of β-methyl-β-ethylacrylic acid (XXXVI) with b.p. 75-77° (26 mm), $n^{17}D$ 1.4430, d^{20}_4 0.9114, in agreement with the literature [8].

β-Methyl-β-ethylacrolein (XXIV). 13.4 g of freshly distilled methylethylethoxyethynyl carbinol (II) in 25 ml of absolute ether was hydrogenated in a jacketed hydrogenation flask, cooled with tap water, in presence of Pd catalyst. Hydrogenation was stopped after 1 hour 20 minutes when 1 mole of hydrogen (2,400 ml; 21°, 745 mm) had been taken up. The catalyst was separated and washed with ether; 20 ml of 5% oxalic acid solution was added and the mixture stirred for an hour. The ethereal layer was separated and the aqueous layer was extracted 3 times with ether. The combined ethereal extracts were washed with 5% sodium bicarbonate solution and dried with calcined magnesium sulfate. Distillation gave 6 g of (XXIV) with b.p. 50-53° (12 mm), $n^{20}D$ 1.4550, d^{20}_4 0.9040, and 3.4 g of a higher boiling fraction with b.p. 56-70° (12 mm), $n^{20}D$ 1.4297.

The 2,4-dinitrophenylhydrazone of aldehyde (XXIV) has m.p. 169-170° (from ethyl alcohol-ethyl acetate mixture); λ_{max} (in isooctane) 352, 365, 380 mμ.

Found %: N 20.05, 20.25. $C_{12}H_{14}O_4N_4$. Calculated %: N 20.10.

Methylisopropenylethoxyethynyl carbinol (IV). 19.8 g (0.236 mole) of freshly distilled methylisopropenyl

* The ultraviolet spectra were measured in the optical laboratory of the Moscow State University.

ketone (III) in 50 ml of absolute ether was stirred while cooling (ice and salt) into the ethoxyethynyl magnesium bromide prepared from 5.2 g of magnesium, 23.4 g (0.214 mole) of ethyl bromide and 15 g (0.214 mole) of ethoxyacetylene in 100 ml of absolute ether. The addition was made in the course of an hour and the reaction mass was then stirred for 30 minutes at 20° and for 15 minutes at 35° before being worked up as above. Yield 18 g of methylisopropenylethoxyethynyl carbinol (IV).

B.p. 66-67° (3 mm), $n^{20}D$ 1.4640, d^{20}_4 0.9468, MR 44.82; calc. 44.39.

Found %: C 69.97, 70.59; H 9.37, 9.45; OH 10.6. $C_9H_{14}O_2$. Calculated %: C 70.20; H 9.10; OH 11.04.

2,3-Dimethylpenta-1,3-dien-5-al (XXV). 12 g of methylisopropenylethoxyethynyl carbinol (IV) in 20 ml of absolute ether was hydrogenated in presence of Pd catalyst. Hydrogenation was stopped after 4 hours when the calculated quantity of hydrogen (1980 ml; 19°, 735 mm) had been absorbed. The catalyst was separated, 10 ml of 3% sulfuric acid was added to the solution, and the mixture was thoroughly stirred for 1 hour. The following fractions were obtained after the usual working-up: 1st, b.p. 55-65° (8 mm), $n^{18}D$ 1.4790, 5.1 g; 2nd, b.p. 65-73° (8 mm), $n^{18}D$ 1.4702, 1.5 g.

Redistillation of the 1st fraction gave 4.5 g of 2,3-dimethylpenta-1,3-dien-5-al (XXV).

B.p. 59-63° (8 mm), $n^{20}D$ 1.4800, d^{20}_4 0.9151, MR 34.15; calc. 33.61.

The 2,4-dinitrophenylhydrazone of aldehyde (XXV) had m.p. 160-161° (from ethyl alcohol-ethyl acetate mixture); λ_{max} (in isooctane) 358, 372, 388 mμ.

Found %: N 19.43, 19.66. $C_{13}H_{14}O_4N_4$. Calculated %: N 19.31.

1-Ethoxyethynylcyclohexan-1-ol (VIII). Dropwise addition of 15.5 g (0.158 mole) of cyclohexanone in 30 ml of absolute ether was made with cooling (ice and salt) to the ethoxy ethynyl magnesium bromide prepared in the usual manner from 3.47 g of magnesium, 15.6 g (0.143 mole) of ethyl bromide and 10 g (0.143 mole) of ethoxyacetylene in 80 ml of absolute ether. The reaction mass was then stirred for 1 hour at room temperature and for 1 hour at 35° before being worked up by the usual procedure. Yield 18.2 g of 1-ethoxyethynylcyclohexan--1-ol (VIII).

B.p. 75-76° (0.02 mm), $n^{20}D$ 1.4830, d^{20}_4 1.0085, MR 47.51; calc. 47.35.

Found %: C 71.42; 71.21; H 9.13, 9.84. $C_{10}H_{16}O_2$. Calculated %: C 71.50; H 9.55.

Cyclohexylideneacetaldehyde (XXVII). 20 g of 1-ethoxyethynylcyclohexan-1-ol (VIII) was hydrogenated in solution in 30 ml of absolute ether in presence of Pd catalyst. Hydrogenation was stopped after 1.5 hours, after absorption of the calculated quantity (3,015 ml; 22°, 751 mm) of hydrogen. The catalyst was separated and 20 ml of 5% oxalic acid was added to the solution. The mixture was vigorously stirred for 1 hour and worked up as usual to give the following fractions: 1st, b.p. 50-52° (2 mm), $n^{20}D$ 1.4880; 7.7 g; 2nd, b.p. 52-60° (2 mm), $n^{20}D$ 1.4670, 3.2 g; residue 5 g.

The 1st fraction was cyclohexylideneacetaldehyde (XXVII) whose 2,4-dinitrophenylhydrazone melted at 194-195° (from ethyl alcohol-ethyl acetate mixture), in agreement with the literature [10]; λ_{max} (in isooctane) 354, 365 mμ.

Found %: N 19.64, 19.70. $C_{14}H_{16}O_4N_4$. Calculated %: N 19.66.

The semicarbazone of aldehyde (XXVII), obtained as a colorless powder, had m.p. 198-199° (from ethyl alcohol); λ_{max} (in isooctane) 273 mμ.

Found %: N 23.10, 22.91. $C_9H_{15}ON_3$. Calculated %: N 23.26.

2,6-Dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X). a) 12.6 g (0.1 mole) of freshly distilled methylheptenone (IX) (b.p. 48-49° at 6 mm) was added in the course of an hour in a nitrogen atmosphere with cooling (ice and salt) to the ethoxyethynyl magnesium bromide prepared from 3.12 g of magnesium, 16 g (0.13 mole) of ethyl bromide and 9.2 g (0.131 mole) of ethoxyacetylene in 75 ml of absolute ether. The reaction mixture was stirred for 1 hour at room temperature and for 30 minutes at 35°. It was then worked up in the usual manner to give 18 g (92%) of 2,6-dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X).

B.p. 79-80° (0.01 mm), $n^{20}D$ 1.4678, d^{20}_4 0.9237, MR 58.98; calc. 58.31.

Found %: C 73.27; 73.41; H 10.17, 10.15. $C_{12}H_{20}O_2$. Calculated %: C 73.41; H 10.20.

b) Into a three-necked flask, fitted with mechanical stirrer, dropping funnel and condenser topped by a calcium chloride tube, were charged 11.2 g of pulverized potassium hydroxide and 60 ml of absolute ether. A mixture of 12.6 g (0.1 mole) of methylheptenone and 8.75 g (0.125 mole) of ethoxyacetylene in 15 ml of absolute ether was added with stirring and iced-water cooling in a nitrogen stream over a period of 1 hour. The mixture was stirred with iced water cooling for 3.5 hours. 15 g of ice was then added, the ether layer was separated and the aqueous layer was extracted 3 times with ether. The ethereal extract was saturated with carbon dioxide. The product was dried with potassium carbonate and distilled to give 3 g of unreacted methylheptenone (b.p. 65-68° at 17 mm, $n^{19}D$ 1.4409) and 11.4 g (58%) of 2,6-dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X) with b.p. 78-80° (0.01 mm), $n^{19}D$ 1.4690.

The yield is lower if the reaction period is lengthened and if the reaction is performed at a higher (room) temperature due to resinification.

Citral (XXVIII). 72.8 g of the above-described 2,6-dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X) was hydrogenated in 100 ml of absolute ether in presence of Pd catalyst while cooling with water. In the course of 3 hours the calculated quantity of hydrogen (9,290 ml; 21°, 753 mm) was taken up and hydrogenation was stopped. The catalyst was separated and 75 ml of 3% sulfuric acid was added to the ethereal solution which had a strong odor of lemon peel. The mixture was shaken for an hour. After working up in the usual manner, the product was distilled in vacuo to give the following fractions: 1st, b.p. 69-71° (1.5 mm), $n^{20}D$ 1.4788, 46 g; 2nd, b.p. 65-79° (1.5 mm), $n^{21}D$ 1.4639, 7.4 g; resinous residue 5.1 g. The 1st fraction was citral; λ_{max} (in heptane) 335 mμ ($\log\epsilon$ 1.54), 347 mμ ($\log\epsilon$ 1.55).

Found %: C 79.02, 78.74; H 10.62, 10.78. $C_{10}H_{16}O$. Calculated %: C 78.90; H 10.52.

Fractional crystallization of the prepared citral from ethyl alcohol led to isolation of the two isomeric 2,4-dinitrophenylhydrazones in a ratio of 8 : 1, orange crystals with m.p. 131-133° and bright-red crystals with m.p. 95-97°.

Crystals with m.p. 131-133°: λ_{max} (in heptane) 253, 364 mμ.

Found %: N 16.64, 16.93. $C_{16}H_{20}O_4N_4$. Calculated %: N 16.88.

Crystals with m.p. 95-97°: λ_{max} (in heptane) 256, 365 mμ.

Found %: N 17.03, 16.87. $C_{16}H_{20}O_4N_4$. Calculated %: N 16.88.

The constants of the 2,4-dinitrophenylhydrazones correspond to those in the literature [11].

The 2nd fraction gives neither a 2,4-dinitrophenylhydrazone nor a semicarbazone; 3 g of this fraction was subjected to exhaustive hydrogenation in 10 ml of absolute ethyl alcohol in presence of Pt catalyst. After 6 hours, 565 ml of hydrogen (20°, 744 mm) had been absorbed, corresponding to 1.5 moles of hydrogen per mole of substance. Distillation gave a liquid with b.p. 65-73° (1.5 mm), $n^{20}D$ 1.4325, consisting mainly of 2,6-dimethyl-8-ethoxyoctan-6-ol.

Found %: C 71.53, 71.49; H 12.58, 13.03. $C_{12}H_{26}O_2$. Calculated %: C 71.30; H 12.88.

Ethyl ester of geranic acid (XXXVIII). A mixture of 13 g of 2,6-dimethyl-8-ethoxy-2-octen-7-yn-6-ol (X), 20 ml of ether and 160 ml of 10% sulfuric acid was stirred for 1.5 hours at room temperature. The temperature of the reaction mass rose to 30°. The ether layer was separated, washed with water until neutral, dried with calcined magnesium sulfate and distilled to give 11.7 g (90%) of the ethyl ester of geranic acid (XXXVIII).

B.p. 68-71° (0.01 mm), $n^{20}D$ 1.4666, d^{20}_4 0.9145, MR 59.51; calc. 58.34.

Found %: C 73.18, 73.13; H 10.62, 10.52. $C_{12}H_{20}O_2$. Calculated %: C 73.41; H 10.20.

Hydrolysis of the ethyl ester of geranic acid with 10% methanolic solution fof potassium hydroxide gave geranic acid in 74% yield; b.p. 93-95° (0.03 mm), $n^{17.5}D$ 1.4780.

Found %: C 71.35, 71.38; H 9.29, 9.49. $C_{10}H_{16}O_2$. Calculated %: C 71.50; H 9.55.

Condensation of ethoxyacetylene with 2-methylhepta-2,4-dien-6-one. Dehydrocitral (XXXIV). 14.1 g (0.114 mole) of freshly distilled 2-methylhepta-2,4-dien-6-one (XXI) ($n^{20}D$ 1.5300) in 30 ml of absolute ether

was added with stirring and cooling (ice and salt) in the course of an hour in a nitrogen stream to the ethoxyethynyl magnesium bromide prepared from 3.56 g of magnesium, 16.5 g (0.152 mole) of ethyl bromide and 10.8 g (0.154 mole) of ethoxyacetylene in 100 ml of absolute ether. The reaction mass was stirred for 1 hour at room temperature and for 35 minutes at 35°. After the usual working-up, the ethereal extract was dried with magnesium sulfate, and the ether was distilled off in a low vacuum in a nitrogen stream at room temperature. The residue was held in a 2 mm vacuum at 25-30° for 1.5 hours. The reaction product was a brownish-yellow oil, weight 20.9 g. A part of this (5.9 g) was distilled in vacuo in a nitrogen stream. 1.8 g of 2,6-dimethyl-8-ethoxyocta-2,4-dien-7-yn-6--ol (XXII) came over. The tarry residue after distillation weighed 3.8 g.

B.p. 83-93° (0.04-0.2 mm), $n^{20}D$ 1.5460, d^{20}_4 0.9699, MR 63.34; calc. 57.78.

Found %: C 73.78, 73.84; H 9.31, 9.21. $C_{12}H_{18}O_2$. Calculated %: C 74.20; H 9.28.

The carbinol (XXII) is an oily, yellow liquid which also decomposes on redistillation. Due to the impossibility of distilling the prepared product without decomposition, its content of carbinol (XXII) was determined by the Chugaev-Tserevitinov method (found 66%).

13.7 g of undistilled product, containing 9.07 g of carbinol (XXII), was hydrogenated in 20 ml of absolute ether in presence of 0.4 g of Pd catalyst. In the course of 2 hours the quantity of hydrogen absorbed was 1132 ml (1 mole) (22°, 739.5 mm). After the usual treatment with 3% sulfuric acid, the product was distilled in vacuo in a nitrogen stream to give the following fractions: 1st, b.p. 45-60° (0.11 mm), 0.45 g; 2nd, b.p. 65-84° (0.11 mm), 6.5 g; tarry residue 4.7 g.

The 2nd fraction was redistilled to give 4.5 g of dehydrocitral (XXXIV) in the form of a yellow liquid with a characteristic odor; b.p. 77-79° (0.23 mm), $n^{19}D$ 1.5681.

The semicarbazone melted at 204-205° after two recrystallizations from methanol; λ_{max} (in methanol), 332, 346 mμ.

Found %: N 20.63, 20.61. $C_{11}H_{17}ON_3$. Calculated %: N 20.28.

The 2,4-dinitrophenylhydrazone melted at 211-212° (from ethyl alcohol-ethyl acetate mixture); λ_{max} (in isooctane) 381, 397, 420 mμ.

Found %: N 16.98, 17.28. $C_{18}H_{18}O_4N_4$. Calculated %: N 16.98.

The above-described semicarbazone and 2,4-dinitrophenylhydrazone did not give a depression of melting point in admixture with the corresponding derivatives of citral obtained by polyenic condensation of dimethylacrolein under the influence of piperidine acetate.

Ethyl ester of dehydrogeranic acid (XLIV). Dehydrogeranic acid. An ethereal extract of 2,6-dimethyl-8--ethoxyocta-2,4-dien-7-yn-6-ol (XXII) was obtained by the above-described procedure from 2.98 g of magnesium, 14.7 g of ethyl bromide, 9 g of ethoxyacetylene and 11.85 g of methylheptadienone (XXI). To the solution was a added 130 ml of 10% sulfuric acid, and the mixture was stirred for 2 hours. After the usual treatment, the product was distilled in a nitrogen stream to give the following fractions: 1st, b.p. 60-67° (0.08 mm), 0.4 g; 2nd, b.p. 88-96° (0.08 mm), $n^{23}D$ 1.5485, 7.6 g; tarry residue 8.6 g.

Redistillation of the 2nd fraction gave 6.3 g of the ethyl ester of dehydrogeranic acid (XLIV) in the form of a greenish liquid; λ_{max} (in isooctane) 307 mμ.

B.p. 86-88° (0.02 mm), $n^{20}D$ 1.5560, d^{20}_4 0.9482, MR 65.89; calc. 57.87.

Found %: C 73.70, 73.94; H 9.39, 9.37. $C_{12}H_{18}O_2$. Calculated %: C 74.17; H 9.28.

Hydrolysis of ester (XLIV) with 2 N sodium hydroxide solution in a nitrogen atmosphere gave a 60% yield of yellow, crystalline dehydrogeranic acid with m.p. 182-183° (from ethyl acetate). The literature reports m.p. 185-186° [12]; λ_{max} (in isooctane) 307 mμ.

Found %: C 72.49, 72.63; H 8.52, 8.47. $C_{10}H_{14}O_2$. Calculated %: C 72.40; H 8.44.

Condensation of benzaldehyde with ethoxyacetylene. 10.2 g (0.096 mole) of benzaldehyde in 15 ml of absolute ether was added dropwise in a nitrogen stream, with stirring and cooling (ice and salt), to the ethoxyethynyl magnesium bromide prepared from 2.3 g of magnesium, 11 g (0.1 mole) of ethyl bromide, and 7 g (0.1 mole)

of ethoxyacetylene in 80 ml of absolute ether. The mixture was stirred for 1 hour at room temperature and for 15 minutes at 35°. After the usual treatment the ethereal extract was divided into two halves. Ether was removed from one portion in vacuo. An attempt to distil the residue in high vacuum in a nitrogen stream led to exothermal decomposition of the substance; at a bath temperature of 140° and a vacuum of 0.02 mm, spontaneous decomposition started with evolution of gas and rise of temperature to 170°. To the second portion of the ether extract was added 135 ml of 10% sulfuric acid. The mixture was stirred for 1 hour and worked up as usual to give 8.4 g of ethyl cinnamate (XLV) with b.p. 83-84° (0.02 mm), $n^{20}D$ 1.5596. Tarry residue 4.2 g.

TABLE 4

Ethoxyethynyl Carbinols

Carbinol No.	Boiling point (pressure in mm)	n_D^{20}	d_4^{20}	Found (%)		Calculated (%)	
				C	H	C	H
(VI)	64—65° (2)	1.4736	0.9590	71.43, 71.05	9.51, 9.44	71.40	9.52
(XII)	94—97 (0.02)	1.4684	0.9234	73.94, 73.88	10.55, 10.57	74.23	10.54
(XIV)	101—103 (0.1)	1.4680	0.9156	74.63, 74.85	10.82, 10.96	74.96	10.78
(XVI)	118—120 (1)	1.4653	0.9024	76.48, 76.51	11.16, 11.01	76.14	11.15
(XVIII)	116—118 (1)	1.4705	0.9147	75.28, 75.21	11.20, 11.16	75.54	11.10
(XX)	105—107 (0.5)	1.4817	1.0430	60.91, 60.83	8.02, 7.87	60.95	7.91

TABLE 5

Aldehydes

Aldehyde No.	Boiling point (pressure in mm)	2,4-Dinitrophenylhydrazones			
		melting point	λ_{max} (m μ) in isooctane	found N (%)	calc. N (%)
(XXVI)	37—38°(0.04)	140—141°	362, 370, 387	18.07, 18.25	18.20
(XXIX)	65—67 (0.01)	74—80	365	16.67, 16.58	16.20
(XXX)	77—80 (0.1)	148—150	365	15.48, 15.41	15.65
(XXXI)	83—85 (0.02)	140—142	255, 365	14.57, 14.63	14.50
		99.5—101	364	14.54, 14.78	
(XXXII)	79—82 (0.2)	157—158	365	14.90, 14.71	14.98
(XXXIII)	80—84 (0.25)	131—133	365, 379	16.01, 15.78	15.97
		102—104	365, 379	15.97, 15.81	

Hydrolysis of ester (XLV) gave cinnamic acid with m.p. 133-135°.

Condensation of ethoxyacetylene with β,β-dimethylacrolein. 23.5 g of freshly distilled β,β-dimethylacrolein in 25 ml of absolute ether was added to the ethoxyethynyl magnesium bromide prepared from 6.1 g of magnesium, 28 g of ethyl bromide and 18 g of ethoxyacetylene in 150 ml of absolute ether. The reaction mass was stirred for 2.5 hours at room temperature and worked-up in the usual manner. The ethereal extract was divided into two halves. The ether was removed from the first part in vacuo at room temperature in a nitrogen stream. Removal of the ether was at once followed by spontaneous decomposition accompanied by rise of temperature to 180°, by evolution of gas and by resinification. 225 ml of 10% sulfuric acid was added to the second portion of ethereal extract. The mixture was stirred for 45 minutes and worked-up in the usual manner.

Vacuum distillation in a nitrogen stream gave 5.3 g of the ethyl ester of δ-methylsorbic acid (XLVII). The tarry residue after distillation weighed 6.5 g.

B.p. 49-52° (0.05 mm), $n^{25}D$ 1.4980, $n^{20}D$ 1.5004, d^{20}_4 0.9432, MR 48.07; calc. 44.48.

Ester (XLVII) is a colorless liquid which turns yellow on standing. Hydrolysis of the ester with a methanolic solution of sodium hydroxide gave a 90% yield of δ-methylsorbic acid with m.p. 109-110° [12].

TABLE 6

Ester No.	Boiling point (pressure in mm)	n^{20}_D	d^{20}_4	Found (%)		Calculated (%)	
				C	H	C	H
(XXXV)	59—60°(27)	1.4375	0.9200				
(XXXVII)	78—80 (80)	1.4827	0.9036	71.69, 71.75	9.30, 9.44	71.40	9.52
(XXXIX)	76—79 (0.02)	1.4671	0.9107	74.27, 74.24	10.60, 10.54	74.23	10.54
(XL)	81—83 (0.05)	1.4669	0.9059	75.25, 75.39	10.81, 11.00	74.96	10.78
(XLI)	93—94 (0.13)	1.4652	0.8971	76.47, 76.55	11.10, 11.25	76.14	11.15
(XLII)	72—74 (0.01)	1.4634	0.9022	75.73, 75.34	11.35, 11.28	75.54	11.10
(XLVI)	83—85 (0.25)	1.4349	0.8986	—	—	—	—
(XLIII)	85—86 (0.2)	1.4778	1.0280	60.96, 61.29	7.72, 7.62	60.95	7.91

The other compounds listed in Tables 1-3 were prepared in similar fashion. Their constants and analyses are presented in Tables 4-6.

SUMMARY

The procedure for preparation of ethoxyacetylene was improved and its condensation with various aldehydes and ketones was described. The resulting ethoxyethynyl carbinols were converted in high yields into the corresponding α,β-unsaturated aldehydes and esters.

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ORGANIC INSECTOFUNGICIDES

XXX. SYNTHESIS OF SOME DERIVATIVES OF 1-METHYLCYCLOPENTANEDIONE-2,3

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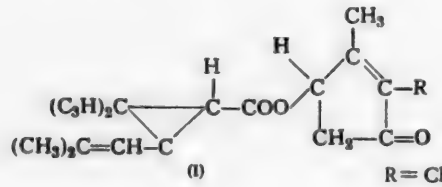
As is known, various pyrethrin preparations, which are practically harmless to warm-blooded animals and man but rapidly affect many harmful insects, have been quite widely used as active contact insecticides. The active principles of these preparations are esters of chrysanthemic acids with 1-methyl-2-alkyl-5-hydroxycyclopenten-1-ones-3 (I), known as pyrethrin-1, pyrethrin-2, cinerin-1 and cinerin-2. However, the preparation of large quantities of these compounds is extremely complicated; the preparation of alletrin and furetrin is somewhat less complicated but they too are very expensive [1].

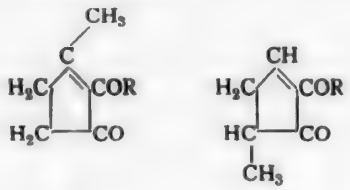


(I)

R = $CH_2CH=CHCH=CH_2$ pyrethrin-1

R = $CH_2CH=CHCH_3$ cinerin-1

In connection with the above, attempts at synthesizing and studying the insecticidal properties of simpler compounds, similar in structure to pyrethrins and cinarins, are continuing. With the aim of finding new active insecticides, we synthesized a series of new esters of the enol of 1-methylcyclopentanedione-2,3, as this diketone is readily available. The esters of 1-methylcyclopentenolone were synthesized by reacting 1-methylcyclopentanedione-2,3 with the acid chlorides of appropriate acids in the presence of potassium carbonate with prolonged heating in hydrophobic organic solvent. Considering the behavior of some cyclic ketones, one would expect that the main reaction products in our case would be compounds with the general formula (II) [2] although traces of compounds with the general formula (III) are also possible.



(II) (III)

The compounds synthesized, and their properties, are given in the table.

Of the compounds we synthesized, only the esters of thiophosphoric acid had insecticidal activity while the esters of carbamic, acetic, butyric and carbonic acids were inactive.

EXPERIMENTAL

We prepared esters of the enol of 1-methylcyclopentanediene-2,3 by the following method: a solution of

the diketone in benzene, dichloroethane or another solvent of the same type was placed in a flask with a reflux condenser, a mechanical stirrer and a dropping funnel; finely powdered, dry potassium carbonate was added and the acid chloride introduced through the dropping funnel, with vigorous stirring and heating. Heating was continued for 8 to 20 hours. After the reaction, the precipitate was filtered and the solvent distilled off. After removal of the solvent, the product obtained was fractionated in vacuum. In most cases the yields did not exceed 50-60%. The compounds synthesized and their properties are listed in the table.

Properties of Compounds (II)

R	Melting point	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	Analysis (%) Found C	Found H	Calculated C	Calculated H
$(CH_3)_2NCO$	58—59.5°	108 (0.2)	—	—	59.26, 59.62	7.55, 7.49	59.0	7.16
$(C_2H_5)_2NCO$	36—38	115—122 (0.3)	—	—	62.85, 62.11	8.42, 8.30	62.54	8.11
CH_3OCO	43—45	96—97 (0.25)	—	—	57.4, 57.13	6.40, 6.46	56.4	5.88
C_2H_5OCO	53—55	103—107 (0.15)	—	—	59.09, 59.46	6.82, 6.68	68.60	6.56
CH_3CO	—	75 (0.075)	—	1.4859	61.66, 61.51	6.83, 6.84	62.30	6.53
C_3H_7CO	—	82.5—85 (0.1)	—	1.4739	65.18, 65.19	7.78, 7.89	65.85	7.74
					% P		% P	
$(CH_3O)_2PS$	—	116—117 (0.2)	1.2562	1.5155	12.51, 12.71		13.10	
CH_3O / C_2H_5O >PS	—	125—127 (0.1)	1.2254	1.5060	12.50, 12.08		12.38	
$(C_2H_5O)_2PS$	—	126—128 (0.2)	1.1715	1.5025	11.72, 11.73		11.75	

SUMMARY

In order to find new active insecticides we synthesized a series of esters of the enol of 1-methylcyclopentanedione-2,3 that had not been described in the literature. On studying the insecticidal properties, we found that the esters of acetic, butyric, carbamic and methoxy- and ethoxycarbonic acids were practically inactive. The esters of dialkoxythiophosphoric acid were active.

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ORGANIC INSECTOFUNGICIDES

XXXI. A NEW METHOD OF PREPARING MIXED ESTERS OF THIOPHOSPHORIC ACID

N. N. Mel'nikov, Ia. A. Mandel'baum and V. I. Lomakina

Recently, a new method was developed in our laboratory for preparing mixed esters of dithiophosphoric acid [1] by reacting aromatic diazo compounds with salts of dialkyldithiophosphoric acid. This method allows the preparation of mixed aliphatic-aromatic esters of dithiophosphoric acid, containing the most varied functional groups in the aromatic radical. It seemed interesting to find out if this method could be applied to the synthesis of esters not only of dithiophosphoric acid, but also mixed esters of monothiophosphoric acid, which are likewise valuable as active insecticides against various pests [2]. A study of the reaction of aromatic diazo compounds with salts of dialkylthiophosphoric acid is especially interesting in connection with the presence of tautomerism and the dual reactivity of the latter [3].

As a result of experiments carried out, it was established that the reaction of aromatic diazo compounds with dialkylthiophosphoric acid salts in an acidic aqueous solution gave a 50% yield of mixed esters of thiophosphoric acid. Under these conditions a mixture of thiol and thione isomers was formed, i.e., the dialkylthiophosphoric acid salts reacted in both of the tautomeric forms and this can be represented by the following general schemes

$$(RO)_2P(=S)CNa + ArN_2X \rightarrow (RO)_2P(=S)OAr + N_2 + NaX$$

$$(RO)_2P(=O)SNa + ArN_2X \rightarrow (RO)_2P(=O)SAr + N_2 + NaX$$

Regarding the observations made by M. I. Kabachnik, S. T. Ioffe and T. A. Mastriukova [4], in our investigations the equilibrium of the tautomeric forms of dialkylthiophosphates is displaced toward the thiol form, as O,O-dialkyl-S-arylthiophosphates predominate in the reaction products and a large amount of the thione isomer is obtained in one case only. We determined the thione isomers in the mixture of esters by oxidation with 55% nitric acid. In this case all the thione sulfur was oxidized to sulfuric acid and was readily determined in the form of barium sulfate.

The results obtained on the thiol and thione isomer contents of the mixed esters of thiophosphoric acid show that not only the reaction medium but also the nature of the attacking agent quantitatively affects the composition of the mixture.

EXPERIMENTAL

We prepared the sodium diethyl thiophosphate in benzene, by A. E. Arbuzov's method, and obtained an 80% yield. The m.p. was 194°. Salts of this quality was used for all experiments on the preparation of mixed esters of thiophosphoric acid.

Preparation of mixed esters of thiophosphoric acid. To illustrate the conditions we used for reacting aryldiazonium salts with sodium diethylthiophosphate, we will describe the preparation of diethylphenylthiophosphate. A solution of phenyldiazonium chloride was prepared in the usual way from 9.5 g of aniline, 25 ml of concentrated hydrochloric acid and 6.9 g of sodium nitrite (in 25 ml of water). Air was passed through the solution obtained for

2 hours (at 0°) to remove the residual nitrous acid. Then a solution of 19.2 g of sodium diethylthiophosphate in 50 ml of water and 2 g of copper sulfate were added to the solution of phenyldiazonium chloride.

After the addition of the copper sulfate, the reaction mixture was gradually heated to 50° and kept at this temperature until the evolution of nitrogen ceased (this required about 1 hour). The mixture was cooled, the oil liberated extracted with ether, the ether solution washed with water and dried over anhydrous calcium chloride and, after removal of the ether, the product obtained was distilled several times in vacuum. After two distillations, a fraction with b.p. 117-123° (0.7 mm) was collected. The yield was about 8.1 g (31%), d^{20}_4 1.1633, $n^{20}D$ 1.5172.

Found %: P 12.1, 12.3; S 12.70, 12.75; C 46.77, 46.83; H 6.70, 6.66. $C_{10}H_{15}O_3PS$. Calculated %: P 12.16; S 13.10; C 46.34; H 6.09.

The other mixed esters of thiophosphoric acid were prepared under exactly the same conditions. The compounds we prepared, and their properties, are listed in the table.

Properties of Mixed Esters of Thiophosphoric Acid $(C_2H_5O)_2PSOAr$

Ar	B.p. (pressure in mm)	d^{20}_4	$n^{20}D$	Isomer content (%)		Analysis (%)			
				P(=S)(O—)	P(=O)(S—)	Found		Calc.	
						P	S	P	S
o-$CH_3C_6H_4$ . .	92—96° (0.3)	1.1319	1.4930	37	63	12.30, 12.30	12.70, 12.80	11.92	12.3
m-$CH_3C_6H_4$ . .	75—80 (0.12)	1.1253	1.5094	44	56	11.32, 11.63	11.80, 11.70	11.92	12.0
p-$CH_3C_6H_4$ . .	127—130 (0.2—0.3)	1.1713	1.5129	55	45	11.73, 11.71	11.80, 11.90	11.92	12.3
p-ClC_6H_4 . . .	119—123 (0.3)	1.2568	1.5298	37	63	10.80, 10.90	12.8,* 12.9	11.00	12.5
p-$CH_3OC_6H_4$.	160—166° (0.6)	1.1547	1.5705	86	14	10.7	--	11.20	–

Determination of thione isomer content. As already indicated above, the thione isomer in the mixture of isomers was determined by oxidation with 55% nitric acid. A sample (0.1-0.2 g) of the preparation was heated with 30-50 ml of 55% nitric acid for 4-5 hours in a water bath with continuous agitation. When a completely clear solution had been obtained, the reaction mixture was diluted with water and the sulfuric acid formed precipitated in the usual way as barium sulfate. (If a turbid solution was obtained on dilution with water, indicating that the oxidation was incomplete, a new sample was taken and the experiment repeated.) Each determination was performed at least twice. For the diethylphenylthiophosphate we obtained a thione sulfur content of 3.08 and 2.81%, indicating a content of 23% O,O-diethyl-O-phenylthiophosphate and 77% O,O-diethyl-S-phenylthiophosphate. Data on the determination of the isomer content of the other esters of thiophosphoric acid are given in the table.

SUMMARY

The reaction of sodium diethylthiophosphate with aromatic diazo compounds was studied. It was shown that sodium diethylthiophosphate reacts with aryldiazonium salts in two tautomeric forms to give mixed esters of thiophosphoric acid.

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*Original Russian pagination. See C. B. translation.

ORGANIC INSECTOFUNGICIDES

XXXII. SYNTHESIS OF SOME MIXED ESTERS OF THIOPHOSPHORIC ACID

Ia. A. Mandel'baum, N. N. Mel'nikov and N. I. Petrova

In 1949 a method was developed in our laboratory for preparing esters of thiophosphoric acid by reacting phosphorus thiotrichloride with alcohols in the presence of caustic alkalis [1]. This method was recently extended to cover the preparation of mixed aliphatic esters of chlorothiophosphoric acid [2]. In order to assess the possibility of using this method for the synthesis of mixed esters of thiophosphoric acid of the aliphatic series, we studied the reaction of mixed dialkylchlorothiophosphates with methyl and ethyl alcohols in the presence of sodium hydroxide. As a result of the experiments, it was established that dialkylchlorothiophosphates react with alcohols in the presence of sodium hydroxide to give good yields of the corresponding trialkylthiophosphates. This reaction may be represented by the following general scheme

$$\begin{matrix} RO \\ R'O \end{matrix}\!\!>\!PSCl + R''OH + NaOH \rightarrow \begin{matrix} RO \\ R'O \end{matrix}\!\!>\!PSOR'' + NaCl + H_2O$$

The compounds we obtained, and their properties, are listed in the table. Almost all the compounds we synthesized have not been described in the literature.

EXPERIMENTAL

Preparation of dimethylalkylthiophosphates. With cooling and vigorous stirring, 45 ml of a solution of sodium hydroxide in 80% methyl alcohol (containing 4.95 g of sodium hydroxide) was added to 0.1 mole of methylalkyl-

Properties of Mixed Esters of Thiophosphoric Acid

Formula	Yield (in %)	Boiling point (pressure in mm)	d_4^{20}	n_D^{20}	P analysis (in %)	
					Found	Calc.
$(CH_3O)_2PSOC_3H_7$-iso	90	79—80° (12)	1.1031	1.4540	16.01, 16.10	16.81
n-$C_4H_9OPS(OCH_3)_2$	84	89—91 (10)	1.0939	1.4561	14.95, 15.10	15.63
iso-$C_5H_{11}OPS(OCH_3)_2$	91.5	96—99 (10)	1.0801	1.4560	14.50, 14.70	14.44
$C_3H_7OPS(OCH_3)(OC_2H_5)$	74.5	58—61 (0.3)	1.1224	1.4540	16.20, 16.40	15.63
$C_4H_9OPS(OCH_3)(OC_2H_5)$	76	60—64 (0.3)	1.0625	1.4490	14.80, 15.10	14.44
iso-$C_4H_9OPS(OCH_3)(OC_2H_5)$	80	64—67 (0.3)	1.0540	1.4470	14.90, 15.10	14.44
iso-$C_5H_{11}OPS(OCH_3)(OC_2H_5)$	64	70—72 (0.25)	1.0645	1.4560	14.20, 14.10	13.45

chlorothiophosphate. During the addition of the sodium hydroxide the temperature was not allowed to rise above 10°. When all the sodium hydroxide had been added, the reaction mixture was stirred at 20° for 2 hours. Then the reaction mixture was diluted with water and the oil which formed was separated, washed with water, dried over anhydrous calcium chloride and vacuum distilled. The distilled preparation was analyzed for phosphorus by a photocolorimetric method [3].

2. Preparation of methylethylalkylthiophosphates. With vigorous stirring and cooling to 0°, 5 g of powdered sodium hydroxide was gradually added to a solution of 0.1 mole of methylalkylchlorothiophosphate in 20 ml of absolute ethyl alcohol. The reaction mixture was then stirred at 20° for 2 hours. After the reaction the mixture was treated with water and the oil was separated, washed with a small amount of water, dried over anhydrous calcium chloride and fractionated in vacuum. The purified preparation was analyzed. The compounds we prepared and their properties are listed in the table.

SUMMARY

A new and simple method was developed for preparing mixed esters of thiophosphoric acid giving 70-94% yields, by reacting dialkylchlorothiophosphates with alcohols in the presence of sodium hydroxide. Most of the compounds synthesized have not been described in the literature.

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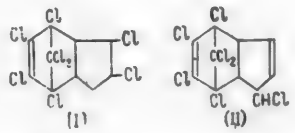
*Original Russian pagination. See C. B. translation.

ORGANIC INSECTOFUNGICIDES

XXXIII. THE SYNTHESIS OF SOME DERIVATIVES OF 4,7-ENDOMETHYLENETETRAHYDROINDAN

S. S. Kukalenko, N. N. Mel'nikov, T. I. Naryshkina and N. I. Shuikin

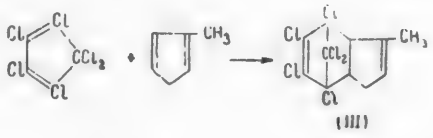
In recent years the chloro derivatives of hydrocarbons, synthesized by a diene reaction from hexachlorocyclopentadiene and various unsaturated compounds [1-3] have been quite widely used in agriculture. The simplest insecticides of this group of compounds are 1,2,4,5,6,7,8,8-octachloro-4,7-endomethylene-3a,4,7,7a-hexahydroindan (I) and 1,4,5,6,7,8,8-heptachloro-4,7- endomethylene-3a,4,7,7a-tetrahydroindan (II), which are known under the trade names of "chlordan" and "heptachlorine."



(I) (II)

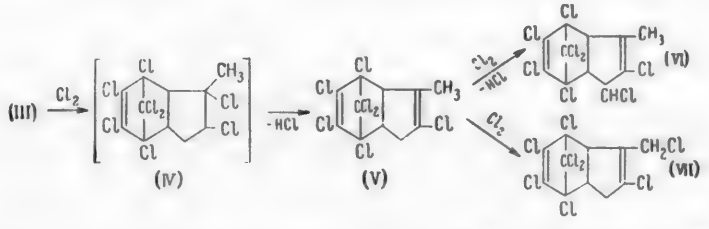
In spite of the fact that these compounds are produced on a large industrial scale, even their closest homologs have not been studied until now. A study of chlordan and heptachlorine homologs undoubtedly would be valuable for investigating the relation of insecticide activity to structure in this series of compounds.

In connection with the above, we undertook a study of the adduct of hexachlorocyclopentadiene with 3-methylcyclopentadiene-2,4. The adduct of hexachlorocyclopentadiene with methylcyclopentadiene was prepared by heating a mixture of the starting substances for a short time at 85-105°. This reaction may be represented by the following scheme



(III)

The adduct obtained under these conditions was a thick, yellowish liquid with a slight, unpleasant smell which distilled in vacuum without decomposition. Chlorination of the adduct in carbon tetrachloride with gaseous chlorine gave a monochloro derivative as the main product, and its formation may be represented by the following scheme



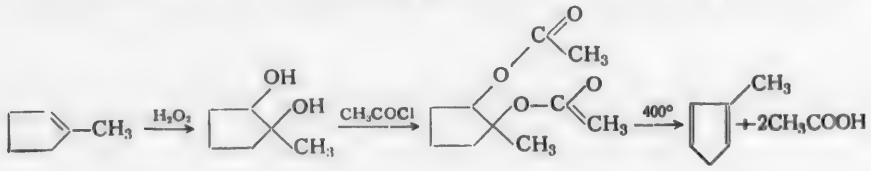
(IV) (V) (VI) (VII)

The chlorination products also contained a small amount of a dichloro-derivative which could be assigned

the structure (IV), (VI) or (VII), though the most probable structure would correspond to formulas (IV) or (VI), as may be deduced by comparison with the behavior of the adduct of hexachlorocyclopentadiene with cyclopentadiene (I). Bromination of the adduct apparently proceeded by a similar scheme as the main product of this reaction was a monobromo-derivative. It is interesting to note that all the derivatives we synthesized have a weaker insecticidal effect than chlordan and much weaker than heptachlorine.

EXPERIMENTAL

1. Synthesis of methylcyclopentadiene. The starting methylcyclopentadiene was synthesized by two methods. One part of it was prepared by catalytic dehydrocyclization [4] of 3-methylpentadene-1,3 (b.p. 76-77°, $n^{20}D$ 1.4460, d^{20}_4 0.7296), which, in its turn, was prepared by dehydration of methylethylvinylcarbinol [5]. The bulk of the methylcyclopentadiene was prepared by another method, namely, pyrolysis of the diacetate of 1-methylcyclopentanediol-1,2, prepared from the corresponding glycol and acetyl chloride by the scheme



The 40 g of methylcyclopentadiene prepared was mainly the β-isomer [4].

B.p. 73-74° (749 mm), $n^{20}D$ 1.4510, d^{20}_4 0.8192.

Found MR_D 26.31. C_6H_8. Calculated: 26.77.

2. Reaction of hexachlorocyclopentadiene with 3-methylcyclopentadiene-2,4. 136.5 g of hexachlorocyclopentadiene was placed in a flask with a reflux condenser, a mechanical stirrer and a dropping funnel and heated to 85° and then 40 g of 3-methylcyclopentadiene-2,4 was gradually added to it from the dropping funnel. The temperature of the reaction mixture rose to 104°. When all the methylcyclopentadiene had been added, the reaction mixture was kept at 100° for 30 minutes and then fractionated in vacuum. We obtained 100 g of 1-methyl--4,5,6,7,8,8-hexachloro-4,7-endomethylene-3,4,7,7a-tetrahydroindan.

B.p. 144-145° (4 mm), d^{20}_4 1.5251, $n^{20}D$ 1.5610, MR_D 74.98; calculated 74.66.

Found %: C 38.13, 37.90; H 2.83, 2.60; Cl 60.94. $C_{11}H_8Cl_6$. Calculated %: C 37.39; H 2.26; Cl 60.34.

3. Chlorination of 1-methyl-4,5,6,7,8,8-hexachloro-4,7-endomethylene-3a,4,7,7a-tetrahydroindan. A stream of dry, gaseous chlorine was passed into a solution of 30 g of 1-methyl-4,5,6,7,8,8-hexachloro-4,7-endomethylene-3a,4,7,7a-tetrahydroindan in 75 ml of dry carbon tetrachloride at room temperature for 50 minutes. During this, the temperature rose from 17° to 35°, after which it began to fall indicating the end of the reaction. After the chlorination the reaction mixture was flushed with dry air (to remove excess chlorine and hydrogen chloride). Then the solvent was removed in vacuum and the substance obtained was fractionated.

1st fraction (20 g), b.p. 150-153° (2 mm), d^{20}_4 1.604, $n^{20}D$ 1.5720, MR_D 79.49; calc. 79.53.
Found %: Cl 64.42. $C_{11}H_7Cl_7$. Calculated %: Cl 64.10.

2nd fraction (10 g), b.p. 167-170° (2 mm), d^{20}_4 1.6460, $n^{20}D$ 1.5764, MR_D 85.25; calc. 84.87.

Found %: Cl 67.38, $C_{11}H_6Cl_8$. Calculated %: Cl 67.00.

It is possible that the substances we obtained were mixtures of stereoisomers, but as yet we have not separated them.

4. Bromination of 1-methyl-4,5,6,7,8,8-hexachloro-4,7-endomethylene-3a,4,7,7a-tetrahydroindan. With cooling to 0° and vigorous stirring, 12.1 g of dry bromine in 50 ml of CCl_4 was gradually added to a solution of 27 g of 1-methyl-4,5,6,7,8,8-hexachloro-4,7-endomethylene-3a,4,7,7a-tetrahydroindan in 50 ml of carbon tetrachloride. During the bromine addition there was a vigorous evolution of hydrogen bromide. At the end of the reaction, the mixture was kept at room temperature for 30 minutes. The reaction mixture was then washed with an aqueous solution of bisulfite and water and dried over calcium chloride; the carbon tetrachloride was distilled

off and the product fractionated in vacuum. The yield was 19 g.

B.p. 167-170° (4 mm), d^{20}_4 1.7406, $n^{20}D$ 1.5880, MR_D 82.99; calc. 82.43.

Found %: C 31.40, 31.67; H 1.75, 1.86. $C_{11}H_7Cl_6Br$. Calculated %: C 30.56; H 1.62.

SUMMARY

It was shown that hexachlorocyclopentadiene reacted with 3-methylcyclopentadiene-2,4 to give an adduct with the composition $C_{11}H_8Cl_6$, and chlorination of it gave mono- and dichloro derivatives. Bromination of the adduct gave a monobromo derivative. None of the compounds synthesized have been described in the literature and are weaker insecticides than chlordan.

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*Original Russian pagination. See C. B. translation.

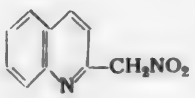
SOME REACTIONS OF 2-NITROMETHYLQUINOLINE

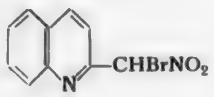
I. SALT FORMATION AND THE ACTION OF HALOGENS

L. Zalukaev and E. Vanags

2-Nitromethylquinoline, which was described previously [1, 2] (I) and has now become a readily accessible compound, was investigated by us from the chemical point of view in more detail. The present work presents data on salt formation and the action of halogens on this nitro compound, which is interesting in many ways.

As could be expected, the methylene group in 2-nitromethylquinoline has an extremely labile hydrogen atom and is highly reactive. The substance dissolved very readily in alkalis to form salts. The potassium salt and even the ammonium salt could be prepared without any special difficulties. The hydrogen atoms in the side chain were substituted by chlorine and bromine at room temperature with exceptional ease to give the corresponding mono- and dihalo derivatives.

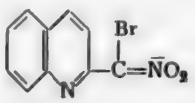

(I)

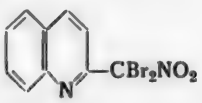

(II)

The preparation of bromonitromethylquinoline was partly described previously [1]. This substance was obtained by treating an acetic acid solution of 2-nitromethylquinoline with bromine in the presence of a small amount of sulfuric acid. On the basis of its high stability to boiling alcoholic potassium hydroxide, a hypothesis was put forward that the halogen atom was aromatically bound. However, further investigations showed that the substance should be assigned formula (II).

Three facts confirm this. Firstly, the substance dissolved readily in alkalis and is recovered unchanged on acidification. Secondly, the substance readily loses a bromine atom when treated with benzoyl chloride. Thirdly, the UV spectra of the monohalo derivatives are similiar in character (Fig. 1) to the spectrum of 2-nitromethylquinoline, whose structure was proved to be (I). This gives grounds for assigning formula (II) to the substance and for noting its exceptional stability to alkalis.

It is probable that the bromine-carbon bond in salts (III) of the nitronic acid is similar in character to an aromatic one. This apparently, explains the capacity of ammonia (for which the capacity for forming nitronic salts is less characteristic) for eliminating a bromine atom from substance (II).


(III)


(IV)

The monochloro derivatives have similiar properties and, in particular, when treated with benzoyl chloride give the same product as monobromo derivatives.

The structure of the dibromo derivative (IV) was confirmed, on the one hand, by its insolubility in alkalis

and, on the other, by its relatively easy conversion to the monobromo derivative. In addition, a comparison of UV spectra (Fig. 2) and solubilities in strong acids also support structure (IV).

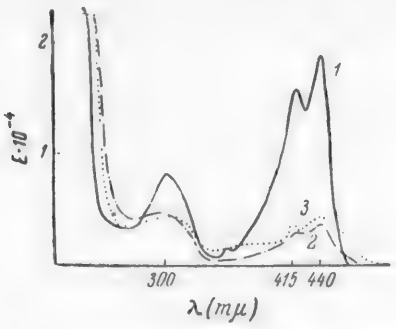


Fig. 1. UV spectra of quinolylnitromethane and its monohalo derivatives. 1) Quinolylnitromethane; 2) monobromoquinolylnitromethane; 3) monochloroquinolylnitromethane.

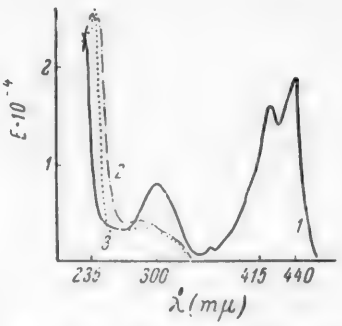


Fig. 2. UV spectra of quinolylnitromethane and its dihalo derivatives. 1) Quinolylnitromethane; 2) dibromoquinolylnitromethane, 3) dichloroquinolylnitromethane.

The situation is similar for 2-dichloronitromethylquinoline. The fact should be noted that chlorine replaced the bromine atom readily in the monobromo derivative to form the dichloro derivative.

The introduction of halogens into the nitromethyl group strongly decreased the basic properties of the quinoline ring as the halo derivatives of 2-nitromethylquinoline are very weak bases and are insoluble in dilute acids.

EXPERIMENTAL

Salts of 2-Nitromethylquinoline

Potassium salt. 1 g of the nitro compound was boiled for 10 minutes on a water bath with 10 ml of an alcohol solution of potassium hydroxide; the 2-nitromethylquinoline was thus converted into a salt. The mixture was cooled and the yellow precipitate separated and recrystallized from alcohol. We obtained 0.95 g of the substance.

Found %: N 12.55; K 16.85. $C_{10}H_7O_2N_2K$. Calculated %: N 12.39; K 17.26.

The salt was readily soluble in water; acidification with acetic acid liberated 2-nitromethylquinoline with m.p. 122-123°.

Ammonium salt. 70 ml of anhydrous alcohol was poured onto 2 g of the nitro derivative and dry gaseous ammonia passed through the mixture for 1 hour. After standing for 5 hours, the precipitate was sucked off and washed with alcohol. We obtained 1.85 g of the ammonium salt with m.p. 136° (decomp.). The salt could be recrystallized from alcohol, but the smell of ammonia was detected. Due to the unusual ease with which the salt was hydrolyzed, data on the nitrogen content were always low.

Found %: N 17.54. $C_{10}H_{11}O_2N_3$. Calculated %: N 20.48.

Acidification of an aqueous solution of the salt liberated the original 2-nitromethylquinoline. If the latter was treated with a methanol solution of picric acid a yellow picrate with m.p. 154-155° (decomp.) was precipitated. Recrystallization from alcohol did not change the melting point.

Found %: N 17.24. $C_{16}H_{11}O_9N_5$. Calculated %: N 16.79.

Upon reaction of the ammonium salt with liquid alkali, ammonia was produced.

Halogen Derivatives of 2-Nitromethylquinoline

2-Bromonitromethylquinoline [1]. 5 g of 2-nitromethylquinoline was dissolved in 50 ml of glacial acetic acid at room temperature and the solution treated with 2 ml of concentrated sulfuric acid and a solution of bromine

in glacial acetic acid. After 5 minutes agitation and subsequent dilution with water, a yellow precipitate formed, which was filtered off, washed with water and recrystallized from alcohol after being dried. We obtained 4.5 g of 2-bromonitromethylquinoline with m.p. 122-123°. The substance was readily soluble in alkalis and was liberated unchanged by acidification with dilute acetic acid. Even boiling it for 30 minutes with 20% potassium hydroxide in alcohol did not produce any change in it.

If some of the substance was heated with benzoyl chloride, brown vapor was liberated and a new product formed, which appeared as colorless plates with m.p. 154° and did not contain bromine. This product could be obtained from 2-nitromethylquinoline and benzoyl chloride. A mixed melting point of the two substances was not depressed and they were identical in all their properties.

Found %: N 8.76; Cl 10.98. $C_{17}H_{13}O_3N_2Cl$. Calculated %: N 8.54; Cl 10.67.

In only one case was it possible to eliminate the bromine atom by passing dry ammonia into a solution of 2-bromonitromethylquinoline in anhydrous ethanol and this gave a product which did not contain halogen. By all the data, the substance was the ammonium salt of 2-nitromethylquinoline described above. It melted at 131-132° and partially lost ammonia during recrystallization from alcohol, but gave more satisfactory nitrogen analysis data before recrystallization.

Found %: N 19.19. $C_{10}H_{11}O_2N_3$. Calculated %: N 20.48.

2-Dibromonitromethylquinoline. One of us described 2-dibromonitromethylquinoline previously [1]. We present data proving its structure.

1 g of 2-dibromonitromethylquinoline was mixed with 30 ml of ethanol and then a stream of dry ammonia passed into the solution. As a result, we obtained the monobromo derivative described above with m.p. 122-123°, which was not depressed by admixture with the authentic product. The 2-dibromonitromethylquinoline was quite readily soluble in concentrated hydrochloric acid and reprecipitated unchanged by dilution with water.

2-Chloronitromethylquinoline. 2 g of 2-nitromethylquinoline was dissolved in 20 ml of glacial acetic acid at room temperature and then a saturated solution of chlorine in the same solvent added. A bright yellow precipitate formed on dilution with water. Recrystallization from glacial acetic acid yielded 0.35 g of yellow needles with m.p. 128-129°.

Found %: N 12.40; Cl 15.37. $C_{10}H_7O_2N_2Cl$. Calculated %: N 12.61; Cl 15.76.

With benzoyl chloride the substance gave a product with m.p. 154°, which was not depressed by admixture with the product from benzoylation of 2-nitromethylquinoline.

2-Dichloronitromethylquinoline. 3 g of 2-nitromethylquinoline was dissolved in 40 ml of glacial acetic acid and a stream of chlorine passed into the solution for 15 minutes. At first the dark yellow solution became almost colorless. The light precipitate, which formed after considerable dilution of the mixture with water, was carefully washed with water and dried. After recrystallization from alcohol, the colorless plates had m.p. 70-72°. The yield was 2.25 g (55%).

Found %: N 11.22; Cl 26.11. $C_{10}H_6O_2N_2Cl_2$. Calculated %: N 10.94; Cl 27.35.

The dichloro derivative did not react with aqueous alkali, but heating on a water bath with a 10% alcohol solution of KOH eliminated one atom of chlorine to give the monochloro derivative. 2-Dichloronitromethylquinoline dissolved in concentrated hydrochloric acid and was precipitated unchanged on dilution of the solution with water.

Action of chlorine on 2-bromonitromethylquinoline. 1 g of the monobromo derivative was treated with a solution of 0.26 g of chlorine in 20 ml of glacial acetic acid. Dilution with water gave a precipitate which weighed 0.9 g and had m.p. 68-70° after drying. The m.p. was 71-72° after the material had been recrystallized from alcohol. The melting point was not depressed by admixture with authentic 2-dichloronitromethylquinoline.

Found %: N 10.92. $C_{10}H_6O_2N_2Cl_2$. Calculated %: N 10.94.

SUMMARY

The salts and 2-halo derivatives of 2-nitromethylquinoline were prepared.

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Institute of Chemistry
Academy of Sciences Latvian SSR

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*Original Russian pagination. See C. B. translation.

VINYLATION OF HYDROBENZOIN. I.

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Vinyl ethers are mainly prepared by the method of A. E. Favorskii and M. F. Shostakovskii [1]. This method is widely used in the Soviet Union and, with certain modifications, abroad [2]. M. F. Shostakovskii et al., [3] and other authors [4] describe the vinylation of polyatomic aliphatic alcohols with acetylene. The vinylation of aliphatic-aromatic and aromatic alcohols with several hydroxyls has not been examined so well.

We investigated the direct vinylation of hydrobenzoin and obtained its full vinyl ether – meso-α,α'-divinyldioxydibenzyl.

EXPERIMENTAL

Preparation of meso-α,α'-divinyldioxydibenzyl. 30 g of hydrobenzoin [5], 300 ml of dioxan and 6 g of potassium hydroxide were placed in a 1 liter rotating autoclave. The acetylene pressure was 15 atm (20°), the vinylation time at 130-135°, 6 hours and the maximum pressure 60 atm. The reaction mixture, which was a brown liquid, was filtered and distilled. We collected a fraction with b.p. 140-165° at 3-4 mm (weight 26 g), which was a constant boiling mixture and deposited fine crystals of the divinyl ether of hydrobenzoin on standing. These were separated and washed with alcohol several times. The yield was 6.4 g (17.1%). After two recrystallizations from alcohol, the melting point was 81-81.6°; the substance distilled at 139-139.5° (1.5 mm) with slight decomposition. The substance formed colorless needles, which were difficultly soluble in cold, but readily soluble in hot alcohol and also in ether, benzene and dioxan.

Found %: C 81.16, 81.01; H 6.59, 6.67. M 260.9. $C_{18}H_{18}O_2$. Calculated %: C 81.17; H 6.81. M 266.3.

Hydrolytic oximination and quantitative hydrogenation indicated the presence of two vinyl groups. The original alcohol was obtained by hydrolysis and a mixed melting point of this with hydrobenzoin was not depressed.

Preparation of meso-α,α'-diethoxydibenzyl. 3 g of the divinyl ether of hydrobenzoin was hydrogenated in 150 ml of alcohol in the presence of 0.3 g of Raney nickel. After separation of the nickel and evaporation of the solution, we obtained 2.7 g of crystals (88.6%). The product was recrystallized three times from alcohol and once from ether, when it had m.p. 66-66.3°; it formed colorless prisms; they were readily soluble in organic solvents and did not react with bromine water.

Found %: C 80.27, 80.03; H 8.26, 8.12. M 267.0. $C_{18}H_{22}O_2$. Calculated %: C 79.96; H 8.20. M 270.4.

Reaction with acetic acid (95%) in the presence of sulfuric acid at 100-110° and subsequent hydrolysis of the diacetate with alcoholic alkali yielded hydrobenzoin, proved by a mixed melting point.

SUMMARY

Hydrobenzoin and acetylene gave meso-α,α'-divinyldioxydibenzyl, which has not been described in the literature. Hydrogenation of it gave meso-α,α'-diethoxydibenzyl.

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Voronezh State University

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A STUDY OF THE EFFECT OF THE REAGENT'S CHARACTER ON THE DIRECTION OF O- AND C-SUBSTITUTION OF METAL DERIVATIVES OF A KETO-ENOL SYSTEM

V. A. Zagorevskii

The purpose of this work, carried out under the direction of A. N. Nesmeianov, was to obtain additional experimental data on the relation of the relative yields of O- and C-derivatives to the character of the reagent, reacting with metal derivatives of a keto-enol system. We investigated the action of a series of halogen derivatives on metal phenolates and β-naphtholates. Furthermore, we reacted sodium phenolate with sulfur trioxide, complexed with dioxan (dioxansulfur trioxide). The results of the main experiments are given in the table.

The Effect of the Reagent's Character on the Direction of O- and C-substitution

Exp. No.	Reagent	Metal derivative	Solvent; temperature	Derivative yields (in %)	
				O	C
1	p-Methoxybenzyl bromide	Sodium β-naphtholate	Acetone, 56-58°	47	24
2	Benzyl bromide	Sodium β-naphtholate	Acetone, 56-58	82	–
3	p-Nitrobenzyl bromide	Sodium β-naphtholate	Acetone, 56-58	87	–
4	Benzyl bromide	Sodium β-naphtholate	Acetone + benzene, 55-57	54	3
5	p-Nitrobenzyl bromide	Sodium β-naphtholate	Acetone + benzene, 55-57	85	Not more than 4
6	4-Bromo-1,3-dinitrobenzene	Sodium β-naphtholate	Boiling dioxan	67	–
7	Benzoyl chloride	Sodium β-naphtholate	Toluene, 100	90	–
8	Acetyl chloride	Dichloroaluminum phenolate	Boiling carbon disulfide	87	–
9	Triphenylmethyl chloride	Sodium phenolate	Boiling dioxan	22	27*
10	Tri-p-nitrophenylmethyl bromide	Sodium phenolate	Boiling dioxan	98	–
11	Dioxansulfur trioxide	Sodium phenolate	Dichloroethane + + dioxan	90-92	–

* Taking into account the "bis-derivative" formed.

As can be seen from the data in the table (exp. 2-5) the introduction of one nitro group into the para-position in benzyl bromide somewhat decreased or, in any case, did not increase the relative yield of C-derivative of β-naphthol.**

** When sodium or lithium β-naphtholates were treated with p-nitrobenzyl bromide in a solution of boiling dioxan, besides O- and C-derivatives, other materials were also formed but these were not investigated closely. p-Methylsulfonylbenzyl bromide reacted similarly with Na-β-naphtholate. Extensive tar formation occurred when 2,4-dinitrobenzyl chloride or iodide reacted with Na-β-naphtholate.

p-Methoxybenzyl bromide (table, exp. 1) showed a much greater tendency for C-substitution. However, it has not been clarified whether in this case the C-p-methoxybenzylnaphthol-2 (I) was a primary substitution product or was formed as a result of O-p-methoxybenzylnaphthol-2 (II) isomerization. Actually, according to our observations, ether (II) may be converted into substance (I) in the presence of p-methoxybenzyl chloride or hydrogen chloride.

In contrast to benzyl bromide [1], 4-bromo-1,3-dinitrobenzene (table, exp. 6) and benzoyl chloride reacted with Na-β-naphtholate in a boiling dioxan medium only at the oxygen atom. The substitution of a slightly polar solvent (toluene) for the dioxan did not change the direction of the benzoylation (table, exp. 7). At the same time, it is known that sodium phenolates and naphtholates are alkylated by such halogen derivatives as benzyl chloride or allyl bromide in slightly polar solvents (toluene, benzene), almost exclusively in the nucleus [2].

The higher tendency of acyl halides to give O-derivatives with metal phenolates was shown in the reaction between acetyl chloride and dichloroaluminum phenolate in a solution of boiling CS_2 (table, exp. 8). O-Acylation can hardly be explained by a specific effect of the solvent, as in the absence of solvent (without heating) [3] or in a boiling benzene medium [4] full aluminum phenolates were converted into esters by acyl chlorides; acylation at a higher temperature gave hydroxyketones (for example [3, 4]).

In contrast to triphenylmethyl chloride, tri-p-nitrophenylmethyl bromide, being a stronger electrophilic reagent, reacted with Na-phenolate exclusively at the O-atom, i.e., without transference of the reaction center (table, exp. 9, 10).

In comparison with the halogen derivatives, dioxansulfur trioxide is an extremely strong electrophilic reagent. It is capable of sulfonating (in a CCl_4 medium) not only anisole (in several minutes) and naphthalene, but also benzene [5]. When sodium phenolate was treated with dioxansulfur trioxide (table, exp. 11) the only reaction product was sodium phenyl sulfate.*

The main results of this work were explained after a thorough examination of the effects of various factors, including the reagent, on the direction of substitution in metal derivatives capable of reacting in two forms [7].

EXPERIMENTAL

Reaction of p-methoxybenzyl, benzyl and p-nitrobenzyl bromides with Na-β-naphtholate in acetone.

a) Reaction with p-methoxybenzyl bromide. The reaction was performed in an atmosphere of nitrogen. 9 ml of a solution of 3.32 g of Na-β-naphtholate in anhydrous acetone was added over a period of 45 minutes to 4.44 g of p-methoxybenzyl bromide (b.p. 107° at 5 mm) [8] in 4 ml of acetone at 56-57° (bath temperature). The mixture was heated for a further 30 minutes at 56-58° and then after cooling, shaken with dilute sulfuric acid and benzene. The organic layer was separated and the solvent evaporated. The residue was separated into neutral and acid fractions using an aqueous methanol solution of potassium hydroxide [1] (first without the use of an organic solvent and then in the presence of petroleum ether). The first fraction was recrystallized from a mixture of benzene and acetone. We obtained 2.5 g (47%) of substance (II), which was insoluble in aqueous and alcoholic alkali and had m.p. 151-151.5°.

Found %: C 82.11, 82.21; H 6.17, 6.09. $C_{18}H_{16}O_2$. Calculated %: C 81.80; H 6.10.

The acid fraction (2.34 g) was recrystallized twice from toluene to give 1.25 g of substance (I), which in all probability was 1-p-methoxybenzylnaphthol-2 with m.p. 130-131°. Substance (I) was soluble in dilute aqueous sodium hydroxide solution.

Found %: C 82.12, 82.28; H 6.32. 6.25. $C_{18}H_{16}O_2$. Calculated %: C 81.80; H 6.10.

b) Reaction with benzyl bromide. The experiment was performed as above. For the reaction we used 3.76 g of benzyl bromide (in 4 ml of acetone) and 9 ml of Na-β-naphtholate solution. One recrystallization of the neutral fraction (4.48 g) from alcohol yielded 3.85 g (82%) of the benzyl ether of β-naphthol with m.p. 98-99°. The melting point of the pure substance was 101-102°. A mixed melting point with an authentic preparation [1] (m.p. 101-102°) was not depressed. After precipitation of β-naphthol with mercury acetate [1], the acid fraction yielded 0.06 g of impure 1-benzylnaphthol-2.

* Phenol also gave phenylsulfuric acid with pyridinesulfur trioxide [6] at 50° and dioxansulfur trioxide [5].

c) Reaction with p-nitrobenzyl bromide. For the reaction we used 4.76 g of p-nitrobenzyl bromide (in 4 ml of acetone) and 9 ml of Na-β-naphtholate solution. The experiment was performed similarly to the previous one with the exception that a 10% aqueous solution of sodium hydroxide was used instead of the alkali in aqueous methanol. We isolated neutral (5.72 g) and acid (0.26 g) fractions. Recrystallization of the neutral fraction from alcohol yielded 4.86 g (87%) of the p-nitrobenzyl ether of β-naphthol with m.p. 109-111°; the pure substance melted at 112.5-113° (from a mixture of alcohol and acetone); it did not depress the melting point of an authentic sample (prepared from Na-β-naphtholate and p-nitrobenzyl chloride in alcohol) [9], m.p. 111.5-112.2° (according to literature data [9] 106.7°). After removal of the β-naphthol, the acid fraction yielded 0.06 g of red-brown crystals, which were apparently impure 1-p-nitrobenzylnaphthol-2.

Reaction of benzyl and p-nitrobenzyl bromides with Na-β-naphtholate in benzene–acetone solution. a) Reaction with p-nitrobenzyl bromide. 9 g of Na-β-naphtholate was dissolved in a mixture of anhydrous benzene and acetone (10 ml of each). 12.5 ml of this solution of naphtholate was added over a period of 2 hours to a solution of 4.42 g of p-nitrobenzyl bromide in 4 ml of acetone and 4 ml of benzene at 55-57° (bath temperature). After 1 hour (same temperature), the reaction mixture was mixed with 0.1 N hydrochloric acid solution and extracted with benzene. The benzene layer was separated and the solvent evaporated. The residue was treated with aqueous methanolic alkali and then subsequently with 10, 5 and 2.5% aqueous sodium hydroxide to give neutral (5.1 g) and acid (0.34 g) fractions. The first was recrystallized from alcohol to give 4.59 g (85%) of the p-nitrobenzyl ether of β-naphthol with m.p. 107-110°; recrystallization from a mixture of methanol and acetone raised the m.p. to 112.5-113°. After removal of the β-naphthol (precipitation of 0.26 g of 1-acetomercurinaphthol-2), the acid fraction yielded 0.2 g of a solid brown mass.

b) Reaction with benzyl bromide. The reaction was performed as above with 3.6 g of benzyl bromide. The residue from evaporation of the benzene was treated with alkali in aqueous methanol. Crystallization of the neutral fraction from alcohol (3.4 g of substance with m.p. 91-94°) and then from methanol gave 2.44 g (54%) of the benzyl ether of β-naphthol with m.p. 101-101.5°. After removal of the naphthol (precipitation of 0.84 g of 1-acetomercurinaphthol-2) and recrystallization from formic acid, the acid fraction yielded 0.14 g (3%) of 1-benzylnaphthol-2 with m.p. 108-111°; the pure substance melted at 111-112°; it did not depress the melting point of an authentic sample [1].

Reaction of p-nitrobenzyl bromide with Li-β-naphtholate. 10 ml of a solution of Li-β-naphtholate in dioxan was added to 2.5 g of p-nitrobenzyl bromide in 10 ml of dioxan * over a period of 2 hours at 103-105° (bath temperature). The mixture was heated for a further 2 hours at 105-116°. As before, acid and neutral fractions were isolated using alkali in aqueous methanol. After precipitation of the β-naphthol with mercury acetate, the first of the fractions yielded 0.4 g (14%) of what in all probability was 1-p-nitrobenzylnaphthol-2 with m.p. 131-132° (from a mixture of benzene and petroleum ether).

Found %: N 4.95, 4.92. $C_{17}H_{13}O_3N$. Calculated %: N 5.01.

The substance formed golden yellow needles, which were readily soluble in dilute solutions of sodium hydroxide. A red salt was formed with strong solutions of the alkali.

Boiling the neutral fraction with alcohol (60 ml) extracted 0.6 g (20%) of the p-nitrobenzyl ether of β-naphthol. Fractional crystallization of the residue from acetone gave two substances with m.p. 242-244° (possibly 4,4'-dinitrostilbene) and 155-157°, which were not examined thoroughly.

Reaction of 4-bromo-1,3-dinitrobenzene with Na-β-naphtholate. The reaction was performed in an atmosphere of nitrogen. A solution of naphtholate, prepared from 0.80 g of β-naphthol and 0.12 g of sodium in 5 ml of dioxan was added over a period of 1 hour to a solution of 1.24 g of 4-bromo-1,3-dinitrobenzene in 5 ml of dioxan at 104-106° (bath temperature). The reaction mixture was heated at the same temperature for a further 0.5 hours; it was then cooled, mixed with 0.1 N hydrochloric acid solution and extracted with ether. The residue left after evaporation of the ether was treated several times with 10% KOH solution. The solid 2,4-dinitrophenyl ether of β-naphthol was washed with water, dried (1.6 g) and treated with ether. We obtained 1.4 g (67%) of the ether with m.p. 92-93°. After recrystallization from benzene, the substance had m.p. 93-94° (according to literature data [10], 95°). Acidification of the alkaline solution and extraction with ether gave 0.1 g of tar.

* With the reverse addition order, considerable tar formation was always observed (especially with Na-β-naphtholate).

Reaction of benzoyl chloride with Na-β-naphtholate. 1.5 g of benzoyl chloride was added to a suspension of Na-β-naphtholate in 15 ml of toluene (the naphtholate was prepared by boiling a toluene solution of 1.6 g of β-naphthol and 0.23 g of sodium and then filtering in a stream of nitrogen), heated on a boiling water bath. The mixture was heated for 1 more hour, diluted with benzene and extracted several times with 10% aqueous sodium hydroxide solution. The alkaline extract was made acid to congo with hydrochloric acid. The organic materials were extracted with ether. The residue from evaporation of the ether was a trace of a red-brown oil. The solvent was evaporated from the neutral solution. We obtained 2.23 g (90%) of β-naphthyl benzoate. It was treated with small portions of ether and then had m.p. 105-106° (according to literature data: [11] 107°, [12] 106°). Benzoylation of Na-β-naphtholate in boiling dioxan in exactly the same way gave only β-naphthyl benzoate.

Reaction of acetyl chloride with dichloroaluminum phenolate. To prepare the dichloroaluminum phenolate [13], a solution of 6.75 g of phenol in 30 ml of CS_2 was added to 9 g of sublimed $AlCl_3$ in 60 ml of CS_2 (vigorous evolution of hydrogen chloride). 5.3 g of acetyl chloride was added in several portions to the solution of phenolate obtained, heated almost to boiling. The solution boiled up. The following day the mixture was decomposed with water. The carbon disulfide layer was separated from the aqueous one and the latter extracted with CCl_4. The combined organic solutions were washed with 10% sodium hydroxide solution (twice with 50 ml each time) and dried. Distillation yielded 8 g (87%) of phenyl acetate with b.p. 190-196°. On redistillation, the substance boiled over the range 192-194° (7 g obtained), while the bulk came over at 194° (according to literature data [14], b.p. 195.7°). The alkaline extract yielded 0.4 g of a liquid (possibly o-acetylphenol).

Reaction of triphenylmethyl chloride with Na-phenolate. A solution of 1.0 g of phenolate in 5 ml of dioxan was added to a solution of 1.40 g of triphenylmethyl chloride in 10 ml of dioxan at 103-105° (bath temperature) over a period of 0.5 hours. The reaction mixture was heated at the same temperature for a further 0.5 hours and treated as described previously [1]. We obtained 0.13 g (8%) of p-hydroxytetraphenylmethane with m.p. 280-282°, 0.55 g (38%) of the triphenylmethyl ether of p-hydroxytetraphenylmethane (bis derivative) with m.p. 201-203° and 0.38 g (22%) of the phenyl ether of triphenylcarbinol* with m.p. 101-102° and 0.3 g of a mixture of the two latter substances.

Reaction of tri-p-nitrophenylmethyl bromide with Na-phenolate. We used 2.3 g of tri-p-nitrophenylmethyl bromide [15] and 1.0 g of Na-phenolate. The reaction was performed exactly as the previous one. A preliminary experiment established that under the given conditions the reaction went to completion and that the phenyl ether of tri-p-nitrophenylcarbinol (III), precipitated in the presence of dioxan, contained dioxan of crystallization. The still hot reaction mixture was diluted with 20 ml of boiling water. The crystals which deposited on cooling were filtered off and dried in a vacuum desiccator over P_2O_5. We obtained 2.45 g of the ether (III) with m.p. 199--200° (decomp.). A solution of 1 g of this product in hot dioxan (about 7 ml) was poured into 25 ml of aqueous methanolic alkali with stirring. After cooling the precipitate was filtered off and washed with alkali and water. It was dried in a vacuum desiccator over solid NaOH. We obtained 1.13 g of (III) (containing dioxan) with m.p. 203-205° (with decomp.). The yield was 98% (allowing for a molecule of dioxan of crystallization). Acidification of the alkaline solution, extraction with ether and benzene and evaporation of the solvents yielded traces of tarry substances. For purification, ether (III) was recrystallized from dioxan and had m.p. 206° (decomp.).

Found %: C 62.35, 62.20; H 4.92, 4.90. $C_{25}H_{17}O_7N_3 \cdot C_4H_8O_2$. Calculated %: C 62.25; H 4.61.

The substance was insoluble in dilute alkalis and a saturated alcohol solution of sodium alcoholate. Gaseous hydrogen was not evolved when (III) was heated with metallic sodium in toluene or dioxan.

To prepare the ether without dioxan of crystallization, 0.6 g of the substance was dissolved in 250 ml of boiling ligroin (120°). Part of the ligroin (about 50 ml) was distilled off. The solution was filtered hot. On cooling it deposited fine, colorless needles. The m.p. was 205.5° (decomp.).

Found %: C 63.91, 63.79; H 3.84, 3.77. $C_{25}H_{17}O_7N_3$. Calculated %: C 63.70; H 3.65.

Hydrolysis of ether (III). A mixture of 0.32 g of ether (III), containing dioxan, 15 ml of alcohol and 1 g of NaOH was heated for several days, then acidified and then phenol extracted from the filtrate with ether and determined as tribromophenol after the usual operations; the yield was 0.17 g (92%) and the m.p. 91-93°. A mixed melting point with an authentic preparation (m.p. 92.5-93.3°) was not depressed. Ether (III) was readily hydrolyzed when

*The phenyl ether of triphenylcarbinol is unchanged under the reaction conditions and therefore it does not isomerize to the C-substituted phenol.

heated for 15 minutes in glacial acetic acid in the presence of concentrated hydrochloric acid and stannous chloride.

Reaction of dioxansulfur trioxide with Na-phenolate. The reaction was performed with the careful exclusion of moisture. The dioxansulfur trioxide [16] was prepared from 3.72 g of sulfur trioxide, 10 ml of dioxan and 20 ml of dichloroethane. The dioxansulfur trioxide dissolved almost completely. Part of this mixture, containing 3.23 g of SO_3, was used for the reaction. With shaking, the dioxansulfur trioxide was added portionwise to a solution of Na-phenolate, prepared by boiling (5 hours) a mixture of 25 ml of dioxan , 5.0 g of phenol and 1.6 g of sodium (the excess sodium was separated by filtration). A white precipitate of sodium phenyl sulfate was rapidly formed. After 3 hours, the reaction mixture (a test for sulfur trioxide with aqueous $BaCl_2$ solution was negative) was mixed with a dilute solution of NaOH and shaken with ether. The aqueous layer was separated, washed with ether and diluted to 250 ml with water. The sulfate ion content of 50 ml of this solution was determined. We obtained 0.02 g of $BaSO_4$, which corresponds to 1.1% of the SO_3 added to the reaction.

The amount of bound phenol was determined quantitatively in another portion (50 ml) of the solution. The cooled solution was made acid to congo with dilute hydrochloric acid. The mixture was extracted several times with ether to remove free phenol. 5 ml of concentrated hydrochloric acid was added to the aqueous solution, which was boiled for 5 minutes and then quickly cooled. The phenol liberated was extracted with ether. The aqueous solution did not decolorize bromine water, indicating that substituted phenol was absent. The phenol was extracted from the ether extract with alkali and precipitated with bromine water in an acid medium. The tribromophenol obtained (2.23 g) was purified by recrystallization from aqueous methanol to give 2.09 g (80%) with m.p. 91-92°.

The amount of sodium phenyl sulfate in 50 ml of the solution was determined quantitatively as the bound sulfuric acid. After the addition of excess barium chloride, the solution was filtered, made weakly acid and mixed with 5 ml of concentrated hydrochloric acid (no precipitate formed in the cold). The mixture was boiled for 5 minutes. We obtained 1.73 g (90%) of $BaSO_4$. The water was removed from another 50 ml portion of the sodium phenyl sulfate solution in vacuum. The crystalline residue was treated with anhydrous alcohol. The alcohol solution was filtered free from undissolved precipitate (it contained sulfate ion) and evaporated in vacuum until crystallization began. The addition of a small amount of ether precipitated colorless, scaly crystals. They were filtered off, washed with alcohol and dried in vacuum desiccator over P_2O_5. We obtained 0.7 g (44%) of sodium phenyl sulfate. The salt was extremely soluble in water, readily soluble in alcohol and hygroscopic [17]. It was hydrolyzed by dilute hydrochloric acid slowly in the cold and rapidly on heating to give phenol and sulfate ion.

0.287 g of the salt in acid $BaCl_2$ solution was boiled for 20 minutes to give 0.327 (95.7%) of $BaSO_4$. Under similar conditions, but in the absence of $BaCl_2$, 0.20 g of the salt was hydrolyzed. We obtained 0.31 g (94.7%) of tribromophenol with m.p. 88-90°. Recrystallization raised the m.p. to 92.5-93.5°.

The dioxansulfur trioxide prepared from 4.2 g of SO_3 in 10 ml of dioxan and 20 ml of dichloroethane, was added in one portion to a solution of phenolate, prepared as previously, starting from 5 g of phenol and 20 ml of dioxan. Heat was evolved. After 3 hours, the precipitate was filtered off, washed twice with absolute ether and dried in a vacuum desiccator over P_2O_5. We obtained 9.47 g (92%) of sodium phenyl sulfate.

Preparation of p-methylsulfonylbenzyl bromide (IV). From a dropping funnel, with an end reaching to the bottom of the flask, 20 g of bromine was added over a period of 10 minutes to 17 g of methyl-p-tolylsulfone at 170-190° (bath temperature); the mixture was heated for 1 hour and dissolved in 50 ml of hot benzene (decolorized with charcoal). On cooling the solution deposited colorless needles of (IV) with m.p. 95-95.8°.

Found %: C 38.70, 38.60; H 3.87, 3.91. $C_8H_9O_2BrS$. Calculated %: C 38.57; H 3.64.

With $AgNO_3$ in alcohol, substance (IV) rapidly gave a precipitate of AgBr and the bromine was quite readily eliminated by heating with alkalis. Reaction with sodium iodide in acetone gave an iodide with m.p. 119-120° (from alcohol). On heating 0.75 g of (IV) with Na-β-naphtholate (from 1 g of β-naphthol and 0.08 g of sodium) in 17 ml of anhydrous alcohol, we obtained 0.5 g (50%) of the p-methylsulfonylbenzyl ether of β-naphthol (V) with m.p. 159-159.5° (from benzene).

Found %: C 69.51, 69.71; H 5.25, 5.35; S 10.05, 10.28. $C_{18}H_{16}O_3S$. Calculated %: C 69.22; H 5.16; S 10.27.

As a result of reacting bromide (IV) with Na-β-naphtholate in boiling dioxan, we obtained ether (V) together with other neutral substances, which were not investigated more closely, and also a reaction product, which was soluble in alkalis and had m.p. 195-197° (from a mixture of benzene and methanol).

SUMMARY

We studied the effect of the reagent's character on the relative yields of O- and C-derivatives, using as examples some alkylation and acylation reactions of phenolates and β-naphtholates.

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SOME ESTERS OF γ-CHLOROCROTYL ALCOHOL

E. L. Gefter

γ-Chlorocrotyl alcohol, obtained by the saponification of 1,3-dichlorobutene-2 [1], is a readily available substance. While the ethers of γ-chlorocrotyl alcohol are well known [1-3], its esters have not been studied (with the exception of the acetate [2]).

With the object of investigating the effect of the γ-crotyl group on some properties of esters we have synthesized a few representatives of this class of compound that have not been described previously. By reacting γ-crotyl alcohol with adipic, sebacic and thiodipropionic acids, and with phthalic anhydride * in the presence of p-toluenesulfonic acid, the corresponding esters were obtained (Table 1).

TABLE 1

γ-Chlorocrotyl Esters of Dibasic Acids

Formula	d_4^{20}	n_D^{20}	Yield (%)
$COOCH_2CH{=}CClCH_3$ $(CH_2)_4$ $COOCH_2CH{=}CClCH_3$	1.1674	1.4818	82
$COOCH_2CH{=}CClCH_3$ $(CH_2)_8$ $COOCH_2CH{=}CClCH_3$	1.1018	1.4778	80
$CH_2CH_2COOCH_2CH{=}CClCH_3$ S $CH_2CH_2COOCH_2CH{=}CClCH_3$	1.1650	1.5095	78
$-COOCH_2CH{=}CClCH_3$ $-COOCH_2CH{=}CClCH_3$	1.2412	1.5380	50

* The preparation of the phthalate ester proceeded much more slowly and required a greater amount of catalyst than in the case of the other esters, and the reaction gave low yields. It seems to us that the low yields of di-γ-chlorocrotyl phthalate (the experiment was repeated with similar results) can be explained by the electronegative nature of the γ-chlorocrotyl group. As a consequence of this, the ester molecules, in which the ester groups occur close together in the alpha-position, form with difficulty. Indirect confirmation of this supposition is given by our unsuccessful attempt to prepare tri-γ-chlorocrotyl phosphate by the interaction of phosphorus oxychloride, γ-chlorocrotyl alcohol, and pyridine. On vacuum distillation, breakdown of the reaction product occurred.

In spite of the presence of two double bonds in the molecule of each of these esters and of rather high boiling points of the esters, the latter were distilled in vacuo, almost to dryness, without polymerizing. This appears to be the natural consequence of a powerful screening of the double bonds in the esters [4].

Comparative data on the boiling points, flash points, and specific resistivities of the esters obtained are given in Table 2, together with those of the known n-butyl esters of the same dibasic acids which are nearest to them (in length of carbon chain).

TABLE 2

Some Properties of γ-Chlorocrotyl and n-Butyl Esters of Dibasic Acids

Substance	Boiling point (pressure in mm)	Flash point	Specific resistivity (in Ω/cm)
Di-γ-chlorocrotyl adipate	160-162° (2.5), 188-189 (4)	193°	$1 \cdot 10^8$
Dibutyl adipate	143 (2-2.5)	157	$2 \cdot 10^{10}$
Di-γ-chlorocrotyl sebacate	208-209 (2-2.5)	216-217	$1 \cdot 10^8$
Dibutyl sebacate	178-180 (1.5-2)	198	–
(Di-γ-chlorocrotyl)-thiodipropionate	200-202 (4)	213	$1 \cdot 10^8$
(Dibutyl)-thiodipropionate	170-171 (3.5-4)	175	$1.4 \cdot 10^{10}$
Di-γ-chlorocrotyl phthalate	189-191 (2-2.5)	201	Less than $1 \cdot 10^8$
Dibutyl phthalate	148 (1), 182 (5)	170	$3.6 \cdot 10^9$

From the data of Table 2 it is evident that substitution of butyl by γ-chlorocrotyl radicals in the dibasic esters brings about an increase in boiling point of 10-15° (at 2-2.5 mm), an increase in flash point of 10-20° and a marked decrease in the specific resistivity (of approximately the second order).

EXPERIMENTAL

γ-Chlorocrotyl alcohol [1]. By reacting 1560 g of 1,3-dichlorobutene-2 with a solution of 1480 g of sodium carbonate in 5.6 liters of water at 70-95° for 5 hours, 900 g (68%) of γ-chlorocrotyl alcohol was obtained.

B.p. 159-161°, 88-90° (50 mm), d^{20}_4 1.1053, $n^{20}D$ 1.4660. Literature data [1]: b.p. 92° (50 mm), d^{20}_{20} 1.106, $n^{20}D$ 1.4652.

γ-Chlorocrotyl adipate. In a three-necked flask fitted with a stirrer, thermometer and L-shaped outlet tube (the latter connected to a condenser and receiver), 100 g adipic acid, 218 g γ-chlorocrotyl alcohol and 2 g p-toluenesulfonic acid were mixed. The mixture was stirred at 95-110° and 70 mm residual pressure (for the more rapid removal of water formed). Esterification was continued for 7 hours (to an Acid Number of 5.6). The reaction mixture was neutralized with 2% alkali solution, washed with water, the water and excess alcohol were distilled off, and the residue was redistilled at 4 mm. The following fractions were taken: 1st fraction, b.p. 60-150°, 10 g; 2nd fraction, b.p. 150-188°, 2 g; 3rd fraction, b.p. 188-189°, 182 g – di-γ-chlorocrotyl adipate. The 3rd fraction was a yellow, clear liquid with an unpleasant odor, soluble in alcohol, ether, benzene and toluene, insoluble in water.

Found %: Cl 21.93. Saponification coefficient 350; acid number 0.3. $C_{14}H_{20}O_4Cl_2$.
Calculated %: Cl 21.94. Saponification coefficient 346.5; acid number 0.0.

γ-Chlorocrotyl Sebacate. The reaction was carried out in the same way as above. By the reaction of 102 g sebacic acid and 160 g γ-chlorocrotyl alcohol in the presence of 3 g p-toluenesulfonic acid at 65-100° and 70-80 mm for 7 hours, 150 g (80%) of di-γ-chlorocrotyl sebacate was obtained. A yellow, clear liquid with an unpleasant odor, soluble in alcohol, ether, benzene and toluene, insoluble in water.

Found %: Cl 18.7. Saponification coefficient 301, 302; acid number 0.26. $C_{18}H_{28}O_4Cl_2$.
Calculated %: Cl 18.69. Saponification coefficient 295.3; acid number 0.0.

γ-Chlorocrotyl thiodipropionate. By the reaction of 60 g thiodipropionic acid and 95 g γ-chlorocrotyl alcohol in the presence of 1 g toluenesulfonic acid at 65-105° and 60-80 mm for 5 hours, 93.5 g (78%) of (di-γ--crotyl)-thiodipropionate. A clear, yellow liquid with a faint, unpleasant odor, soluble in alcohol, ether, benzene and toluene, insoluble in water.

Found %: Cl 19.8. Saponification coefficient 321; acid number 0.4. $C_{14}H_{20}O_4Cl_2S$.
Calculated %: Cl 19.96. Saponification coefficient 315; acid number 0.0.

γ-Chlorocrotyl Phthalate. By the reaction of 153 g phthalic anhydride and 328 g γ-chlorocrotyl alcohol in the presence of 7 g p-toluenesulfonic acid at 90-110° and 70-75 mm for 12 hours, 172 g (50%) of di-γ-chlorocrotyl phthalate was obtained. A clear, yellow-orange, odorless liquid, solidifying at 14-15° to light-yellow crystals, soluble in alcohol, ether, benzene and toluene, insoluble in water.

Found %: Cl 20.43. Saponification coefficient 319; acid number 0.3. $C_{16}H_{16}O_4Cl_2$. Calculated %: Cl 20.66. Saponification coefficient 326.3; acid number 0.0.

Determination of the flash points of the esters was carried out (by the Brenken method) in an open cup. The specific resistivity was measured according to GOST 6581-53.

SUMMARY

Some previously unknown esters of γ-chlorocrotyl alcohol and dibasic acids have been prepared and characterized.

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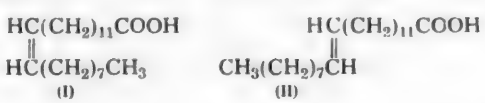
THE CONFIGURATIONAND PROPERTIES OF UNSATURATED ACIDS AND THEIR DERIVATIVES

VIII. THE REACTIVITY OF ERUCIC AND BRASSIDIC ACIDS AND THEIR ESTERS

A. K. Plisov and N. V. Bulatova

Examination of the properties of erucic and brassidic acids, and also of their esters, is of definite interest. The characteristic properties, connected with the spatial structure of the octadecenic acids and their esters were investigated sufficiently in a number of previous papers [1]. The necessity is therefore quite obvious for a similar systematic study of the reactions of erucic and brassidic acids and their esters, according to the position of the double bond, and also of reactions connected with the ester group. Hydrogenation, oxidation and saponification reactions are involved in this connection. On the basis of a study of these reactions the question of the configuration of erucic and brassidic acids, which up to the present time has not been established reliably by chemical means, can be clarified.

On the basis of determination of the cryoscopic constants, Mascarelli [2] attributed to erucic acid the cis--configuration (I), and to brassidic acid the trans-configuration (II).



(I) (II)

G. V. Pigulevskii and P. A. Artamonov [3], taking into account the difference in the frequencies of the Raman spectra due to the double bonds, also decided that erucic acid has the cis, and brassidic acid the trans-structure. Assuming that in the given case the spatial structure must show up in the chemical transformations of these acids we carried out the experiments described below. The results confirm the conclusion made on the basis of the physical methods, relegating erucic acid to the cis-series and brassidic acid to the trans-series. Erucic acid and its esters hydrogenate and oxidize more rapidly than brassidic acid and its esters, but erucates saponify more slowly than brassidates.

EXPERIMENTAL

Isolation of erucic acid from rapeseed oil. In distinction from the known methods of isolating erucic acid from fatty oils [4], we used the following method for its preparation from rapeseed oil, based on the good solubility of lead erucate in hot alcohol. To the mixture of fatty acids isolated from 200 g of rapeseed oil dissolved in 200 ml alcohol and heated on a water-bath, a boiling solution of 80 g of lead acetate in 100 ml alcohol was added. After boiling for a short time the solution was transferred to a well-heated separating funnel in which it was allowed to settle for 1-1.5 minutes. Then the liquid mass of lead salts of saturated acids, insoluble in hot alcohol, were separated from the solution and washed 2-3 times with 50-75 ml of boiling alcohol for the removal of coprecipitated lead erucate. The alcohol washings were combined with the main portion and kept for 7-8 hours at 2-3°. The clear solution was then decanted from the separated lead erucate and the latter decomposed with dilute hydrochloric acid (1 : 5). The supernatant oily layer of crude erucic acid, formed by heating and salting out, was washed with hot water and recrystallized from a 3-4-fold volume of alcohol.

Brassidic acid was obtained by the action of oxides of nitrogen on erucic acid according to the method of Holde [5].

The methyl and butyl esters of erucic and brassidic acid were prepared by direct esterification of the acids (1 ml) by the corresponding alcohol (3 ml) in the presence of conc. H_2SO_4 (1% on the fatty acid). The butyl ester of brassidic acid, not described in the literature, was prepared by us for the first time.

Found: acid number 0; saponification number 142.4. $C_{26}H_{50}O_2$. Calculated: saponification number 142.17.

The physical constants of the substances investigated are quoted below (Table 1).

TABLE 1

	Erucic acid	Brassidic acid	Methyl erucate	Methyl brassidate	Butyl erucate	Butyl brassidate
Melting point	34°	61°	–	34-35°	–	33-35°
Boiling point	–	–	220-221° (at 5 mm)	224° (at 5 mm)	244° (at 7 mm)	246° (at 7 mm)
n_D	1.4473 (at 55°)	1.4460 (at 58°)	1.4558 (at 20°)	1.4490 (at 35°)	1.4555 (at 20°)	1.4549 (at 20°)

The erucic and brassidic acids and their methyl and butyl esters (1 mole) were oxidized with $K_2Cr_2O_7$ (1.5 moles) in glacial acetic acid at the same temperature in each case. The course of the reaction was followed by determination of the unreacted oxidizing agent by iodometric titration of the reaction mixture. A weighed sample of the substance (1/2000 mole, i.e., 0.1691 g of the acids, 0.1761 g of the methyl esters and 0.1977 g of the butyl esters) was dissolved in glacial acetic acid in a 10 ml measuring flask, the solution transferred to a flask with a ground-glass stopper and the measuring cylinder washed out with 3 ml of the solvent. [After the solution of isomer stood in a thermostat at 55 or 40° for half an hour and a solution of the oxidizing agent stood in a jacketed burette (also heated with water at 55 or 40°), 87 ml of the oxidizing agent solution was added to the solution of the substance to be oxidized.]. Immediately after mixing the solutions, the first determination of the oxidizing agent content in the reaction mixture was carried out (initial concentration).

The oxidation reaction rate constant was calculated from the equation

$$K = \frac{2.303}{t} \log \frac{\alpha}{\alpha - x},$$

where: α is the initial oxidizing agent concentration in percent (100%), and x is the quantity of oxidizing agent reacted after time t.

Data for the oxidation of erucic and brassidic acids and their esters are given in Table 2.

In order to examine the question of the course of the oxidation reaction 3.4 g of erucic and brassidic acids in glacial acetic acid was oxidized with $K_2Cr_2O_7$ (4.5 g) under the conditions described above. On completion of oxidation the reaction product was neutralized and evaporated to dryness. The residue was decomposed with dilute sulfuric acid and steam-distilled. Since about 1 g of pelargonic acid, identified by its melting point (12.5°) and refractive index ($n^{20}D$ 1.4306), was found in the steam distillates, it can be presumed that the oxidation of erucic and brassidic acids, under our chosen conditions, follows the same course, and is associated with scission of their molecules at the double bond.

Catalytic hydrogenation of erucic and brassidic acids, methyl erucate, methyl brassidate, butyl erucate and butyl brassidate was carried out simultaneously in hydrogenation flasks at 23°. Mechanical agitation was performed by means of a magnetic stirrer. Pd on $BaSO_4$ from the same preparation was used as catalyst; the solvent was ethyl acetate. 1/2000 mole of isomer in 5 ml ethyl acetate was added to the catalyst, saturated with hydrogen (0.02 g Pd/$BaSO_4$ or 0.0005 g Pd) in 3 ml ethyl acetate in a stream of hydrogen. The results of hydrogenation are given in Table 3.

The hydrogenation reaction rate constants are calculated from the equation

$$K = \frac{2.303}{t} \log \frac{\alpha}{\alpha - x},$$

where: α is the quantity of hydrogen required for complete saturation of the sample in percent; $\alpha - x$ is the quantity of hydrogen combined with the sample after time t, in percent.

TABLE 2

Oxidation of Erucic and Brassidic Acid and Their Esters with $K_2Cr_2O_7$ in Acetic Acid at 55 and 40°.

t (in hours)	Erucic acid		Brassidic acid		Methyl erucate		Methyl brassidate		Butyl erucate		Butyl brassidate	
	x	K	x	K	x	K	x	K	x	K	x	K
15	43.9	0.039	28.3	0.022	29.2	0.023	18.4	0.014	28.1	0.022	17.8	0.013
21	53.2	0.036	34.7	0.020	39.6	0.024	26.0	0.014	34.7	0.020	21.6	0.012
30	63.0	0.033	41.2	0.018	45.0	0.020	31.4	0.013	43.4	0.019	27.1	0.011
64	83.0	0.036	65.7	0.018	71.1	0.020	52.1	0.012	67.3	0.019	45.0	0.010
80	95.1	0.038	73.8	0.017	80.4	0.020	61.9	0.012	76.6	0.019	53.2	0.010
108	100	—	85.8	0.018	91.3	0.022	77.1	0.014	86.9	0.019	67.3	0.010
136	—	—	92.3	0.019	100	—	91.2	0.017	92.8	0.019	79.8	0.011
	$K_{av}^{55°}=0.036$		$K_{av}^{55°}=0.018$		$K_{av}^{55°}=0.021$		$K_{av}^{55°}=0.013$		$K_{av}^{55°}=0.019$		$K_{av}^{55°}=0.011$	
	$K_{av}^{40°}=0.019$		$K_{av}^{40°}=0.011$		$K_{av}^{40°}=0.012$		$K_{av}^{40°}=0.008$		$K_{av}^{40°}=0.0094$		$K_{av}^{40°}=0.007$	
Activation energy	8363		8183		8297		7660		8986		7386	
Probability constant	$1.1 \cdot 10^8$		$8.56 \cdot 10^7$		$1.01 \cdot 10^8$		$3.85 \cdot 10^7$		$2.91 \cdot 10^8$		$2.54 \cdot 10^7$	

TABLE 3

Hydrogenation of Erucic and Brassidic Acids and their Esters in the Presence of Pd at 23°

t (in min)	Erucic acid		Brassidic acid		Methyl erucate		Methyl brassidate		Butyl erucate		Butyl brassidate	
	$\alpha-x$	K	$\alpha-x$	K	$\alpha-x$	K	$\alpha-x$	K	$\alpha-x$	K	$\alpha-x$	K
60	8.26	0.0014	5.7	0.0010	6.6	0.0011	3.3	0.0006	3.3	0.0006	—	—
120	16.5	0.0015	9.9	0.0008	13.2	0.0012	7.3	0.0006	9.0	0.0008	4.9	0.0004
450	44.6	0.0012	33.8	0.0008	34.7	0.0009	24.7	0.0006	33.8	0.0009	19.8	0.0005
810	66.1	0.0014	57.7	0.0010	56.2	0.0011	44.6	0.0007	52.8	0.0009	32.2	0.0005
1550	95.0	0.0019	87.6	0.0010	91.7	0.0016	72.7	0.0008	90.9	0.0015	56.2	0.0005
1800	100	—	91.7	0.0013	—	—	81.7	0.0009	—	—	61.9	0.0006
	$K_{av}=0.0014$		$K_{av}=0.0009$		$K_{av}=0.0011$		$K_{av}=0.0007$		$K_{av}=0.0009$		$K_{av}=0.0005$	

The hydrogenation of erucic and brassidic acids has already been described in the literature [6]. However, repetition of this was necessary for solution of the problem of the effect of the alcohol radical on the rate of hydrogenation. Moreover, the figures obtained by Paal [6], characterizing the rate of hydrogenation of oleic and elaidic acids seem to us to be somewhat approximate. In Paal's paper it is stated that oleic acid, for example, after 60 minutes absorbs about half as much hydrogen as erucic acid. This does not agree with the hydrogenation experiments on oleic and erucic acids repeated by Fokin [7]. The data obtained by one of us [1] on the hydrogenation of oleic acid and its esters confirms that erucic acid and its esters hydrogenate more slowly than oleic acid and its esters. The same applies to elaidic and brassidic acids and their esters.

Reduction of erucic and brassidic acids with hydriodic acid. For clarification of the results of the combination of hydrogen with erucic and brassidic acids in the absence of a catalyst, experiments were carried out on their re-

duction with a solution of HI. The experiments consisted in heating equal weights of the acids (6 g) to 110-115°, with HI solution, in high-melting sealed tubes for 30 hours (intermittent). After it separated from the reaction mixture, the reduction product was dissolved in a small quantity of petroleum ether and the bromine number was determined [8]. It was found that 95% of the erucic acid and 99% of the brassidic acid remained unchanged. When the erucic acid reduction product was treated with cold alcohol at 5° the erucic acid went into solution, and the residue after recrystallization from petroleum ether corresponded in acid number and melting point (82°) to behenic acid. The crude product from the reduction of erucic acid can be elaidinized. This reaction is not given by the brassidic acid reduction product. Hence under the conditions of uncatalyzed reduction of erucic and brassidic acids isomerization does not take place and the reduction of erucic acid in this case also is more rapid than that of brassidic acid.

Saponification of the methyl and butyl esters of erucic and brassidic acids was carried out under conditions described previously [9], in small beakers with lids containing sealed-in platinum electrodes. The course of saponification was followed by the change in electrical conductivity of the reaction mixture, the fall in which corresponded to the decrease in concentration of hydroxyl ions expended on saponification of the esters. The commencement of the reaction was taken as the moment of addition of the alcoholic KOH solution to the alcoholic solution of the isomer. The electrical conductivity was calculated from the resistance measured with an SK ohmmeter with an indicator lamp. Equal weights of the esters (1/1000 mole or 0.3522 g for the methyl and 0.3946 g for the butyl esters) were dissolved in 9 ml of 96% alcohol and kept in a thermostat for half an hour at 25°. 1 ml of 1N alcoholic KOH was then added to the ester solution and the first determination of alkali content carried out immediately.

TABLE 4

Saponification of the Methyl and Butyl Esters of Erucic and Brassidic Acids at 25°

t (in hours)	Methyl erucate			Methyl brassidate			Butyl erucate			Butyl brassidate		
	Electrical conductivity	x	K	Electrical conductivity	x	K	Electrical conductivity	x	K	Electrical conductivity	x	K
0	303	—	—	303	—	—	303	—	—	303	—	—
5	278	8.1	0.00017	232	20.0	0.0005	283	6.7	0.0001	240	20.6	0.0005
17	244	19.5	0.00014	177	41.6	0.0004	255	15.9	0.0001	195	36.6	0.0003
21	229	24.4	0.00013	154	49.3	0.0005	244	19.3	0.0001	185	38.9	0.0003
30	213	29.5	0.00014	148	51.3	0.0004	236	22.2	0.0001	172	43.2	0.0003
44	159	35.3	0.00015	134	55.9	0.0003	224	26.4	0.0001	170	43.6	0.0002
	$K_{av} = 0.00015$			$K_{av} = 0.0001$			$K_{av} = 0.0001$			$K_{av} = 0.0003$		

The saponification reaction rate was calculated from the equation for a 2nd-order reaction

$$K = \frac{1}{t} \frac{x}{\alpha(\alpha - x)},$$

where: α is the initial electrical conductivity in percent (100%), x is the decrease in electrical conductivity after time t.

Results of experiments on the saponification of the methyl and butyl esters of erucic and brassidic acids are given in Table 4.

SUMMARY

1. A method for the isolation of erucic acid from rapeseed oil is proposed.

2. The butyl ester of brassidic acid, not described in the literature, has been prepared.

3. It is shown that erucic acid and its esters oxidize and hydrogenate more rapidly than the corresponding brassidic acid and its esters.

4. It is shown that the saponification of erucates proceeds more slowly than that of brassidates.

5. The oxidation, hydrogenation and saponification reactions of erucic and brassidic acids and their esters, in conformity with the spatial configurations, confirm the cis-structure of erucic acid and the trans-structure of brassidic acid.

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Odessa State University

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THE CONFIGURATION AND PROPERTIES OF UNSATURATED ACIDS AND THEIR DERIVATIVES

IX. THE PROPERTIES OF THE α-METHYLCROTONIC ACIDS AND THEIR ESTERS

A. K. Plisov and N. P. Paladienko

In a previous communication [1], one of us has already shown that the α-methyl crotonic acids (angelic and tiglic), and also their esters, do not display the same reactivity. This was established by the example of the oxidation and saponification reactions. In these cases it was shown that angelic acids and its esters, as in all cases with other unsaturated acids described previously, oxidize at the double bond considerably more rapidly than tiglic acid and its esters, whereas saponification of the esters, on the other hand, proceeds more slowly with the former than with the latter. However Crüros [2] in the hydrogenation of angelic and tiglic acids found conditions under which the former acid (cis-form) hydrogenates more slowly than the latter (trans-form). However, the quantity of catalyst used in these experiments exceeded that normally used, being some hundreds of times greater than the latter.

These circumstances served as a basis on which to widen our investigation of the α-methylcrotonic acids and to examine, in particular, their behavior on hydrogenation. This reaction has been described in considerable detail by one of us [3] in the case of crotonic acid and its esters, and obtaining such data for the α-methylcrotonic acids and their esters, in addition to clarifying other problems, should make it possible to decide the effect of the methyl group on this reaction. The presence of this group, in our opinion, must to some extent affect the rate of addition of hydrogen to the double bond.

The realization of such observations seems the more essential in that the α-methylcrotonic acids are analogous, in a number of their chemical reactions, to the crotonic acids, the configuration of which has been established by the method of combination dispersion of light.

With regard to differences in the reactivity of the cis- and trans-forms in the given case, this is explained by the fact that the space near the double-bond of the trans-form is occupied on both sides by groups of atoms, the volume of which is considerably greater than that of the hydrogen atom, and for the cis-form this space is less occupied on one side. It must be pointed out that the carboxyl group occupies the space near the double bond to a greater extent (its volume calculated by Kopp's formula is 36.5 cm^3/mole) than does the methyl radical (volume 27.6 cm^3/ mole). Steric hindrance, created by substitution at the double bond can be illustrated also by planar projections of the cis- (I) and trans-(II)-methylcrotonic acids (Fig. 1). The planar projections were constructed in conformity with the additivity rule, with conservation of the proportionality of the atomic radii, valence angles and length of bonds between the atoms.

We prepared the stereo-isomeric α-methylcrotonic acids and their ethyl, butyl, isobutyl and benzyl esters. The acids and esters were hydrogenated. The data so obtained are in full agreement with those of our previous papers [1]. The graphs (Figs. 2-4) show the course of hydrogen absorption by the acids and esters at two temperatures. Attention is attracted in the first place, to the fact that hydrogenation of the α-methylcrotonic acids proceeds more slowly than that of crotonic acid. In other words, the methyl group in the α-position to the carboxyl, evidently hinders addition of hydrogen to the double bond.

The results of these experiments fully coincide with the conclusions drawn previously in relation to the hydrogenation of the cis- and trans-forms of unsaturated acids and their esters [3]. The cis-forms hydrogenate more easily than the trans-forms. Furthermore, all the esters of the α-methylcrotonic acids hydrogenate with more difficulty than the acids themselves.

On comparing the hydrogenation rates it was noted that the free acids hydrogenate with the greatest difference in rates and their esters with the least difference. It is also of interest that the differences in hydrogenation rates show up to a greater extent on comparing the results of hydrogenation of the various esters of tiglic acid with one another and to a lesser extent in the case of the esters of angelic acid.

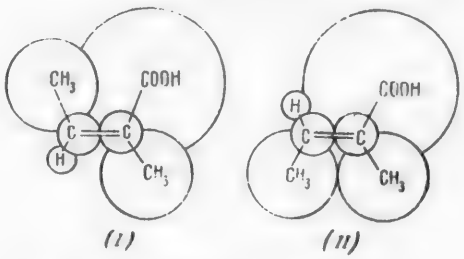

Fig. 1. Planar projection of α-methylcrotonic acid. I) Cis-acid; II) trans-acid.

From examination of the graphs, the effect of the size of the alcohol radical on the hydrogenation rate is also notable: the greater the volume of the alcohol radical, the slower the rate of hydrogenation of the ester.

Hydrogenation of the stereoisomeric α-methylcrotonic acids and their esters proceeds in an analogous manner with both palladium and platinum catalysts. A temperature reduction of 10° markedly reduces the rate of hydrogen addition.

In order to examine the nature of the addition of hydrogen to the α-methylcrotonic acids, experiments on the reduction of angelic and tiglic acids with hydriodic acid solution were carried out. In these uncatalyzed reduction experiments, the phenomena connected with adsorption on a metal are eliminated, and the results indicate an inherent difference in the aptitudes of the α-methylcrotonic acids with respect to the rate of hydrogen addition, as was established by the experiments, described above, on catalytic hydrogenation.

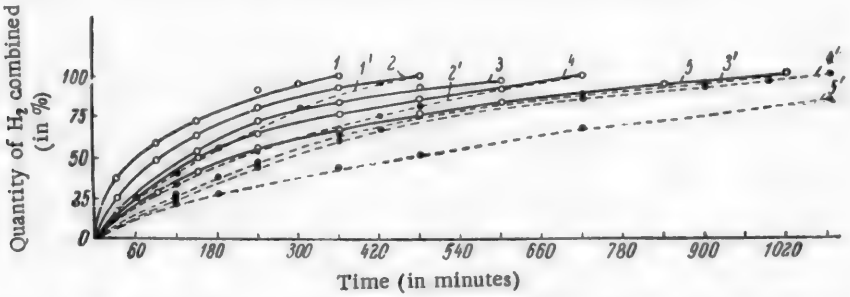

Fig. 2. Hydrogenation of angelic and tiglic acids and their esters on a Pd-catalyst at 25° in anhydrous ethanol. 1) Angelic acid; 2) ethyl angelate; 3) butyl angelate; 4) isobutyl angelate; 5) benzyl angelate; 1') tiglic acid; 2') ethyl tiglate; 3') butyl tiglate; 4') isobutyl tiglate; 5') benzyl tiglate.

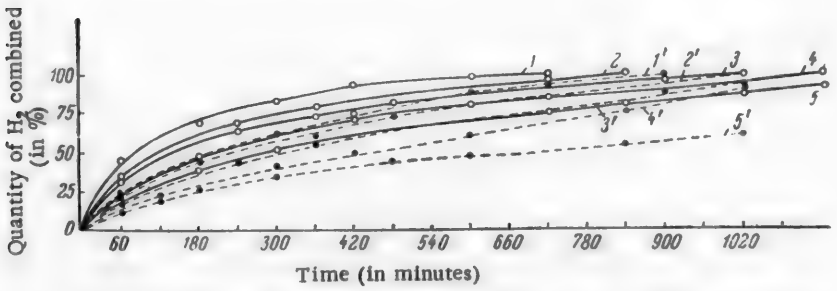

Fig. 3. Hydrogenation of angelic and tiglic acids and their esters on a Pd-catalyst at 15° in anhydrous ethanol. 1) angelic acid; 2) ethyl angelate; 3) butyl angelate; 4) isobutyl angelate; 5) benzyl angelate; 1') tiglic acid; 2') ethyl tiglate; 3') butyl tiglate; 4') isobutyl tiglate; 5') benzyl tiglate.

Thus the results of our experiments presented here, and also experiments described in other communications [4] confirm that angelic acid and its esters have the cis-configuration and tiglic acid and its esters correspond to the trans-configuration.

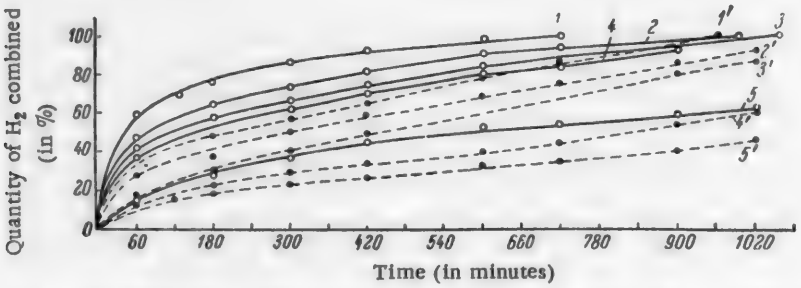

Fig. 4. Hydrogenation of angelic and tiglic acids and their esters on a Pt-catalyst at 25° in anhydrous ethanol. 1) Angelic acid; 2) ethyl angelate; 3) butyl angelate; 4) isobutyl angelate; 5) benzyl angelate; 1') tiglic acid; 2') ethyl tiglate; 3') butyl tiglate; 4') isobutyl tiglate; 5') benzyl tiglate.

EXPERIMENTAL

Angelic and tiglic acids were prepared as previously described by us [1].

Ethyl angelate was prepared from potassium angelate and ethyl iodide [5]. Liquid, b.p. 140-141°, $n^{24}D$ 1.4280, d^{12}_{12} 0.9276. Yield 38%.

Butyl angelate, not previously described in the literature, was prepared for the first time by us under the same conditions as for ethyl angelate. Liquid, b.p. 73-74° at 9 mm, d^{12}_{12} 0.9089, $n^{20}D$ 1.4350. Yield 40%.

Isobutyl angelate was prepared for the first time by us from the salt and the halogen derivative. B.p. 176-177°, $n^{20}D$ 1.448, d^{14}_{14} 0.8974. Yield 30%.

Benzyl angelate has not been reported in the literature. It was prepared as above. B.p. 125-126° at 6-7 mm, $n^{12}D$ 1.510, d^{12}_{12} 1.0366, d^{12}_{4} 1.0361. Yield 47%.

Ethyl tiglate was prepared by esterification [5] in the form of a liquid with an odor of fennel. B.p. 154°, $n^{12}D$ 1.440, $n^{25}D$ 1.4364, d^{12}_{4} 0.9349. Yield 78.1%.

Butyl tiglate has not been reported in the literature. We prepared it by esterification, as for ethyl tiglate. B.p. 189-191°, $n^{12}D$ 1.442, $n^{15}D$ 1.440, d^{12}_{12} 0.9141. Yield 72.5%.

Isobutyl tiglate has not been reported in the literature. We prepared it by esterification. B.p. 182-184°, $n^{12}D$ 1.439, $n^{18}D$ 1.437, d^{12}_{12} 0.9047. Yield 60%.

Benzyl tiglate has not been reported in the literature. It was obtained by us from potassium tiglate and benzyl chloride in anhydrous methanol after heating on a boiling water-bath for 24 hours. B.p. 139° at 9 mm, $n^{20}D$ 1.518, d^{12}_{12} 1.0431. Yield 56.5%.

All the esters prepared by us had an acid number of 0 and the saponification coefficients agreed with theory (within the limits of experimental error).

Hydrogenation was carried out at 25 and 15° with supported Pt and Pd catalysts. The hydrogenation apparatus, which has been described previously [3] allowed experiments to be carried out on five pairs of isomers simultaneously. In each experiment 0.0005 mole of substance was taken for hydrogenation, in 2 ml anhydrous ethyl alcohol. Hydrogenation was carried out in the presence of 0.0200 g catalyst. All experiments were conducted at atmospheric pressure, which fluctuated in different experiments between 768 and 754 mm.

Isolation and examination of the hydrogenation products consisted in removing the catalyst and solvent and subsequent application of the normal methods of purification of methylethylacetic acid and its esters. In all cases

methylethylacetic acid and its ethyl, butyl and isobutyl esters, with constants in full agreement with the literature data, were isolated from the hydrogenation products.

Reduction of the α-methylcrotonic acids with hydriodic acid. Equal quantities of HI solution were placed in high-melting glass tubes and equal weights (0.3 g) of the α-methylcrotonic acids were added. The sealed tubes with their contents were heated at 110-115° for 24 hours. After opening the tubes and isolating the reaction products it was found (by titration with a solution of bromine in potassium bromide) that the angelic acid had reacted to the extent of 6%, and the tiglic to 1%

SUMMARY

1. The butyl and benzyl esters of angelic acid and the butyl, isobutyl and benzyl esters of tiglic acid, not previously reported in the literature, have been prepared for the first time.

2. It is shown that angelic acid and its esters hydrogenate more rapidly than tiglic acid and its esters.

3. The existence of an influence by the alcohol radical on the course of the hydrogenation reaction is established.

4. A difference is shown in the effect of the alcohol radical of the cis- and trans-esters on the hydrogenation reaction.

5. Differences in the relative rates of hydrogenation of the α-methylcrotonic acids and their esters confirm the classification of angelic acid and its esters in the cis-series and tiglic acid and its esters in the trans-series.

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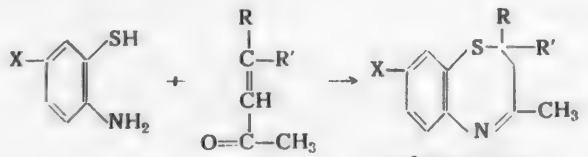
THE CONDENSATION OF o-AMINOTHIOPHENOLS WITH UNSATURATED KETONES AND β-HALOKETONES. II

L. K. Mushkalo

In the first communication it was shown [1] that on condensation of o-aminothiophenols with mesityl oxide, and also with methyl-β-bromoisobutyl ketone, derivatives of dihydrobenzohepta-1,5-thiazine are formed.

Syntheses of new derivatives of heptathiazone are described below. o-Aminothiophenol, 5-nitro-2-aminothiophenol, N-methyl-, N-ethyl- and N-phenyl-o-aminothiophenols were used as amino components in the condensation. Of the unsaturated ketones the following were used for the reaction: mesityl oxide, ethylideneacetone and methylvinyl ketone. The formation of seven-membered, heterocyclic ring compounds from the aminothiols, not substituted at the nitrogen atom, proceeds according to the scheme:



R & R′ = H, CH_3; X = H, NO_2.

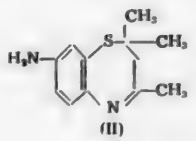
(I)

Condensation of the aminothiols takes place most easily with mesityl oxide. With ethylideneacetone and especially with methylvinyl ketone the yield of condensation products is considerably lower.

The nitro group in position 5 in the aminothiophenol retards the condensation reaction. Thus, for example, on condensation of 5-nitro-2-aminothiophenol with mesityl oxide the yield of 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine (I) ($X = NO_2$; R and $R' = CH_3$) is only 13%. As a rule the yield of heptathiazines increases when, instead of unsaturated ketones, the corresponding β-haloketones are used in the condensation with aminothiols, and this is particularly valuable for the condensation of nitroaminothiophenols. For example, on condensing 5-nitro-2-aminothiophenol with methyl-β-bromoisobutyl ketone the yield of the bromohydrate of 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine (I) ($X = NO_2$; R and $R' = CH_3$) exceeds 70%.

On condensing 6-nitro-2-aminothiophenol with ethylideneacetone we were completely unsuccessful in isolating the corresponding nitroheptathiazine. When methyl-β-bromopropyl ketone was used for this reaction the yield of the hydrobromide 2,4-dimethyl-8-nitrodihydrobenzohepta-1,5-thiazine (I) ($X = NO_2$; $R = CH_3$, $R' = H$) was 40%.

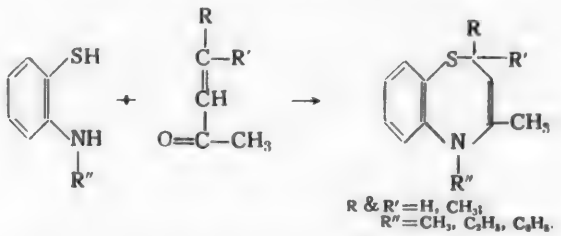
On reduction of 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine with tin in hydrochloric acid, the corresponding amine 2,2,4-trimethyl-8-aminodihydrobenzohepta-1,5-thiazine (II), was formed in 75% yield.



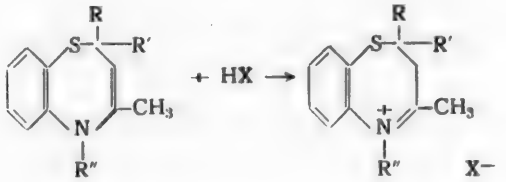
(II)

The same sort of qualitative difference in closing the seven-membered, heterocyclic ring is found with N-substituted o-aminothiophenols. Here also condensation with mesityl oxide proceeds easily. With methylvinyl ketone the yield of condensation products is quite insignificant.

The nature of the radical attached to the nitrogen atom of the aminothiols exerts a substantial effect on the yield of condensation products. It was established that the highest yield of heptathiazines is obtained when N-phenyl--o-aminothiophenol is used for condensation with unsaturated ketones. Thus, for example, on condensation of N--phenyl-o-aminothiophenol with methylvinyl ketone, the yield of base is 68%, whereas with the N-alkyl-o-aminothiophenols the yield of the corresponding heptathiazine base is only 16-30%.



When the bases obtained were heated with mineral acids, the quaternary salts were obtained in quantitative yields.



Usually the perchlorates, which can easily be isolated in the crystalline state, are obtained. The corresponding quaternary chlorides are obtained by saturating a benzene solution of the base with hydrogen chloride. These quaternary salts are difficult to crystallize. They form a glassy mass, deliquescing in the air. They are quite suitable for preparing cyanine dyes.

EXPERIMENTAL

2,4-Dimethyldihydrobenzohepta-1,5-thiazine. A mixture of 11.2 g o-aminothiophenol and 7.5 g of ethylideneacetone was heated in a sealed tube, on the water bath, for 3 hours. The reaction product was dissolved in ether, washed with aqueous alkali, dried over solid potassium hydroxide and redistilled in vacuo. 7.5 g, or 44%, of a fraction boiling at 125-128° and 5 mm was collected. In a repeated redistillation a fraction consisting of pure 2,4-dimethyldihydrobenzohepta-1,5-thiazine was collected.

B.p. 115-118° at 2 mm, d^{20}_{20} 1.1147, $n^{20}D$ 1.60683.

Found %: N 7.36; S 16.58. $C_{11}H_{13}NS$. Calculated %: N 7.33; S 16.75.

The picrate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine was obtained by mixing equivalent quantities of alcoholic solutions of the base and of picric acid. The picrate, recrystallized from alcohol had m.p. 157°.

Found %: N 13.31, 13.41. $C_{17}H_{16}O_7N_4S$. Calculated %: N 13.33.

2,2,4-Trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine. A mixture of 3 g 5-nitro-2-aminothiophenol and 2 g of mesityl oxide was heated in a sealed tube for 3 hours at 130°. The reaction product was then dissolved in ether and washed with aqueous alkali. After the ether was evaporated the residue consisted of a dark resin which crystallized after addition of a few drops of alcohol and rubbing with a glass rod. The crystals were filtered off and recrystallized from alcohol. 0.6 g (13.6%) of pure 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine were obtained in the form of light-yellow prisms with m.p. 114°.

Found %: N 10.90, 10.82. $C_{12}H_{14}O_2N_2S$. Calculated %: N 11.10.

2,2,4-Trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine hydrobromide. A mixture of 10 g 5-nitro-2-aminothiophenol, 10 g freshly redistilled methyl-β-bromoisobutyl ketone and 100 ml methyl alcohol was heated on the water bath until all the nitroaminothiophenol went into solution. This required 15-20 minutes. The methyl alcohol was then evaporated down in an evaporating dish on the water bath to $^1/_3$ volume. The hydrobromide of 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine crystallized out from the residue on cooling. Yield 13 g (71%); m.p. 188°. A further quantity of impure product could be isolated from the mother liquor.

Found %: N 8.38, 8.35; Br 23.90, 23.92. $C_{12}H_{15}O_2N_2SBr$. Calculated %: N 8.46; Br 24.11.

The base isolated from this salt was shown to be identical with 2,2,4-trimethyl-8-nitrodihydrobenzohepta-5-aminothiophenol. A mixture of the two, as for the pure base, had m.p. 114°.

2,4-Dimethyl-8-nitrodihydrobenzohepta-1,5-thiazine hydrobromide. From 3.4 g 5-nitro-2-aminothiophenol, 3.3 g freshly redistilled methyl-β-bromopropyl ketone and 25 ml methyl alcohol, 2.5 g (39.4%) of the hydrobromide of 2,4-dimethyl-8-nitrodihydrobenzohepta-1,5-thiazine was obtained by an analogous method, having m.p. (from alcohol) 186°.

Found %: N 8.87, 8.89. $C_{11}H_{13}O_2N_2SBr$. Calculated %: N 8.83.

2,2,4-Trimethyl-8-aminodihydrobenzohepta-1,5-thiazine. To a solution of 1 g 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine hydrobromide in 8 ml concentrated hydrochloric acid, was added 1.5 g granulated tin. After evolution of heat had ceased the mixture was heated on the water bath until the tin had completely dissolved. The crystalline precipitate that formed was decomposed with aqueous alkali to a strongly alkaline reaction. The amine was extracted with ether, dried over solid potassium hydroxide and recrystallized from alcohol after evaporating off the ether. The yield of amine was 0.45 g or 75%. M.p. 140°.

Found %: N 12.78, 12.73. $C_{12}H_{16}N_2S$. Calculated %: N 12.72.

2,2,4-Trimethyl-8-acetaminodihydrobenzohepta-1,5-thiazine hydrochloride. The hydrochloride prepared by saturating an ethereal solution of 2,2,4-trimethyl-8-aminodihydrobenzohepta-1,5-thiazine with hydrogen chloride, was dissolved in acetic anhydride, with heat. On cooling, crystals of the hydrochloride of the acetyl derivative of the amine were deposited. M.p. 210°.

Found %: N 9.56, 9.52. $C_{14}H_{19}ON_2SCl$. Calculated %: N 9.40.

On adding ammonia to an aqueous solution of the hydrochloride of the acetyl derivative, free 2,2,4-trimethyl-8-acetaminodihydrobenzohepta-1,5-thiazine was obtained, having m.p. 150°.

Found %: N 10.63, 10.62. $C_{14}H_{18}ON_2S$. Calculated %: N 10.69.

2,4,5-Trimethyldihydrobenzohepta-1,5-thiazine. A mixture of 9.3 g N-methyl-o-aminothiophenol and 5.6 g ethylideneacetone was heated in a sealed tube on the water bath for 4 hours. The reaction product was extracted with ether, washed with alkali and redistilled in vacuo at 2 mm after evaporating off the ether. 6 g (43%) of a fraction boiling at 120-126° was collected. 2,4,5-Trimethyldihydrobenzohepta-1,5-thiazine is a colorless liquid; d^{20}_{20} 1.0909, $n^{20}D$ 1.5911.

Found %: N 6.66, 6.92. $C_{12}H_{15}NS$. Calculated %: N 6.83.

The methylperchlorate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine was formed by mixing the base obtained with 30% perchloric acid. The quaternary salt, recrystallized from alcohol had m.p. 111°.

Found %: N 4.77; Cl 11.95. $C_{12}H_{16}O_4NSCl$. Calculated %: N 4.58; Cl 11.62.

The chloromethacrylate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine was formed on saturating a benzene solution of the base with hydrogen chloride. This quaternary salt was obtained in the form of a glassy mass. It was not isolated in the crystalline state.

2,4-Dimethyl-5-ethyldihydrobenzohepta-1,5-thiazine. A mixture of 8 g N-ethyl-o-aminothiophenol and 4.5 g ethylideneacetone was heated on the water bath for 2 hours. The condensation product was then washed with alkali, extracted with ether and dried over solid potassium hydroxide. After evaporating off the ether the residue was redistilled in vacuo at 2 mm and 130-138°. The yield of 2,4-dimethyl-5-ethyldihydrobenzohepta-1,5-thiazine

was 6 g (50%); d^{20}_{20} 1.0657; n_D 1.57078.

Found %: N 6.15; S 14.06. $C_{13}H_{17}NS$. Calculated %: N 6.11; S 14.00.

The ethylperchlorate of 2,4-dimethyldihydrobenzohepta-1,5-thiazine was obtained by mixing the base with 30% perchloric acid. The crystals of the quaternary salt which separated out were recrystallized from alcohol. The melting point of the quaternary salt was 170°.

Found %: N 4.39; Cl 11.32. $C_{13}H_{18}O_4NSCl$. Calculated %: N 4.38; Cl 11.11.

4,5-Dimethyldihydrobenzohepta-1,5-thiazine. On mixing 7.1 g N-methyl-o-aminothiophenol with 3.6 g methylvinyl ketone the mixture warmed up and formed an emulsion (as a result of the formation of water). The mixture was heated on the water bath for 2 hours. The reaction product was then dissolved in ether, washed with alkali, dried over solid potassium hydroxide and redistilled in vacuo. 2.9 g (30%) of a fraction boiling at 100-103° and 6 mm was collected. 4,5-Dimethyldihydrobenzohepta-1,5-thiazine is a colorless oil; d^{20}_{20} 1.0921, $n^{20}D$ 1.60143.

Found %: N 7.42; 7.30. $C_{11}H_{13}NS$. Calculated %: 7.33.

The methylperchlorate of 4-methyldihydrobenzohepta-1,5-thiazine. On mixing 4,5-dimethyldihydrobenzohepta-1,5-thiazine with 50% perchloric acid, crystals of the quaternary salt were formed, with m.p. 100.5°.

Found %: N 4.77, 4.43; Cl 12.20. $C_{11}H_{14}O_4NSCl$. Calculated %: N 4.79; Cl 12.18.

4-Methyl-5-ethyldihydrobenzohepta-1,5-thiazine. On mixing 7.2 g N-ethyl-o-aminothiophenol with 3.3 g methylvinyl ketone the mixture warmed up and formed an aqueous emulsion. After heating for 3 hours in a sealed tube on the water bath, the reaction product was washed with alkali and extracted with ether. The ethereal solution was dried over solid potassium hydroxide, the ether distilled off and the residue redistilled in vacuo. 1.6 g (16%) of a fraction collected between 125 and 130° at 10 mm consisted of pure 4-methyl-5-ethyldihydrobenzohepta-1,5-thiazine; d^{20}_{20} 1.1103, $n^{20}D$ 1.58223.

Found %: N 6.87, 6.90. $C_{12}H_{15}NS$. Calculated %: N 6.83.

The ethylperchlorate of 4-methyldihydrobenzohepta-1,5-thiazine was prepared by mixing 4-methyl-5-ethyldihydrobenzohepta- 1,5-thiazine with 50% perchloric acid. The quaternary salt isolated crystallized out after two days. Colorless crystals with m.p. 131°.

Found %: N 4.56, 4.50; Cl 11.63. $C_{12}H_{16}O_4NSCl$. Calculated %: N 4.58; Cl 11.62.

The chloroethylate of 4-methyldihydrobenzohepta-1,5-thiazine was prepared by saturating a benzene solution of the base with hydrogen chloride. This quaternary salt was a glassy mass, deliquescing in the air.

The condensation of N-phenyl-o-aminothiophenol with methylvinyl ketone. A mixture of 3 g N-phenyl-o--aminothiophenol and 1.1 g methylvinyl ketone was heated in a sealed tube on the water bath, for 3 hours. Drops of water appeared in the upper part of the tube. The condensation product was treated with alkali, extracted with ether, dried over solid potassium hydroxide and the ether distilled off on the water bath. The residue, weighing 3.2 g, was mixed with 50% perchloric acid. After rubbing with a glass rod, crystals of the phenylperchlorate of 4-methyldihydrobenzohepta-1,5-thiazine, weighing 3 g (68%), separated. M.p. 162-163°.

Found %: N 3.89, 3.93; Cl 9.83. $C_{16}H_{16}O_4NSCl$. Calculated %: N 3.96; Cl 10.04.

SUMMARY

1. By condensing α,β-unsaturated ketones and β-haloketones with o-aminophenylmercaptans the following new derivatives of dihydrobenzohepta-1,5-thiazine were obtained: 2,4-dimethyl-, 2,2,4-trimethyl-8-nitro-, 2,4-dimethyl-8-nitro-, 2,4,5-trimethyl-, 2,4-dimethyl-5-ethyl-, 4,5-dimethyl-, 4-methyl-5-ethyl- and 4-methyl--5-phenyldihydrobenzohepta-1,5-thiazine.

2. By reduction of 2,2,4-trimethyl-8-nitrodihydrobenzohepta-1,5-thiazine, the corresponding amine, 2,2,4-trimethyl-8-aminodihydrobenzohepta-1,5-thiazine, was obtained.

3. From N-alkyl and N-phenyldihydrobenzohepta-1,5-thiazines and mineral acids, the following quaternary salts of dihydrobenzohepta-1,5-thiazine were obtained in quantitative yields: the methylperchlorate of 2,4-dimethyl-, the ethylperchlorate of 2,4-dimethyl, the methylperchlorate of 4-methyl-, the ethylperchlorate of

4-methyl- and the phenylperchlorate of 4-methyldihydrobenzohepta-1,5-thiazine.

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Kiev State University

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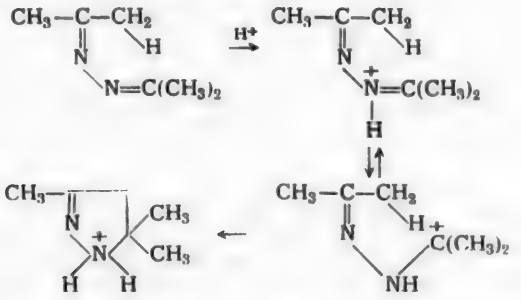
THE REACTIONS OF HYDRAZINE DERIVATIVES

XVIII. THE ACTION OF ACIDIC REAGENTS ON AZINES

A. N. Kost, I. I. Grandberg and E. B. Evreinova

The conversion of azines to pyrazolines under the action of acids [1, 2] or alkyl halides [3, 4] has been reported in a number of previous communications.

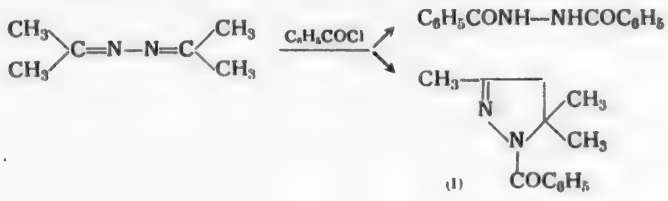
The mechanism of this cyclization is evidently analogous to the mechanism of the aldol condensation. In the formation of aldols (in acid media) the first step is the addition of a proton to the oxygen of the carbonyl group, with the formation of a carbocation. The latter reacts with a second molecule of aldehyde and then splits off the proton. Similarly azines readily take up a proton, the ammonium ion isomerizing to carbonium, thus making cyclization possible. In contrast to the aldol condensation the proton does not split off at the end of the reaction because of the formation of a stable pyrazoline ion.



Information on the action of acyl halides on azines is extremely contradictory. Thus, Minunni [5] observed that benzaldazine, under the action of benzoyl chloride, is converted to benzaldehyde benzoylhydrazone, but furfural azine breaks down, giving dibenzoylhydrazine. On the other hand Lochte [6] reported that acetone azine cyclizes with the same reagent, to form 1-benzoyl-3,5,5-trimethylpyrazoline (I). According to the data of Benary [7] cyclohexanone azine is converted, by the action of acyl halides, to the 1-acyloctahydrocarbazole (with splitting off of ammonia). Finally, it is stated that acetophenone azine does not react with acyl halides [7].

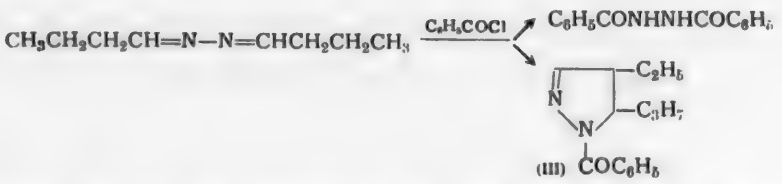
We have confirmed Benary's findings as regards the conversion of cyclohexanone azine to the octahydrocarbazole but we were unable to extend this reaction to other azines (with the object of synthesizing homologs of pyrrole).

From acetone azine and benzoyl chloride we obtained a substance with m.p. 236°, identical with that described by Lochte, but it proved to be not benzoylpyrazoline (I), but sym-dibenzoylhydrazine. However benzoylpyrazoline (I) can be obtained by the action of benzoylchloride on acetone azine in the total absence of moisture, but this substance has completely different properties (m.p. 93°) and was characterized by us for the first time [8].

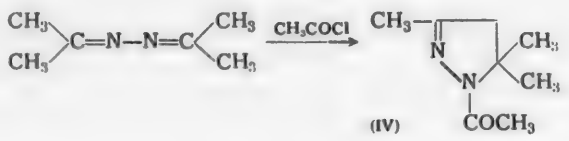


We have found a similar phenomenon (the cleavage of azines with the formation of sym-diacylhydrazines) by the action of benzoyl chloride on the azines of methylisopropyl ketone and cyclopentanone (II).

By the action of benzoyl chloride on butyraldazine (as for acetone azine), 1-benzoyl-4 ethyl-5-propylpyrazoline (III) was obtained together with dibenzoylhydrazine.



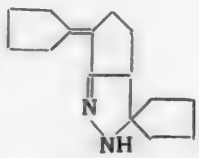
Cyclopentanone azine (II) reacts exothermically with acetyl chloride, but in this case we succeeded in isolating only sym-diacetylhydrazine. With acetone azine, on the other hand, only the product of cyclization was obtained, i.e., 1-acetyl-3,5,5-trimethylpyrazoline (IV).



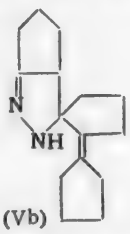
For the purpose of confirming the structure of the compounds formed, in addition to elementary analysis, comparison of constants and, where necessary, synthesis by another method, we characterized the substances by the absorption spectra,* shown in Figs. 1 and 2.

The course of the reaction (cleavage or cyclization) depends not only on the nature of the azine and the acylating agent, but also on the conditions. Thus, if there are traces of moisture in the reaction mixture, cleavage of the azine takes place preferentially.

We have stated earlier [9] that cyclopentanone azine (II), under the action of oxalic acid, is converted to the compound (V) with m.p. 140°, differing in properties from 3,4-trimethylene-5,5-tetramethylene pyrazoline (VI). This substance (V) has the composition $C_{15}H_{22}N$, is soluble in acids and gives picrate and benzoyl derivatives. On carrying out the cyclization of cyclopentanone azine (II) with anhydrous formic acid,** the same substance (V) was isolated together with cyclopentanone formylhydrazone (VII). In contrast to the absorption spectrum of the pyrazoline (VI) the absorption maximum in the spectrum of substance (V) is displaced toward the red end of the spectrum (Fig. 3), which can be explained by the presence of a conjugated system of double bonds. From these considerations we consider that substance (V) has the structure (Va) or (Vb), the former being the more probable.



(Va)

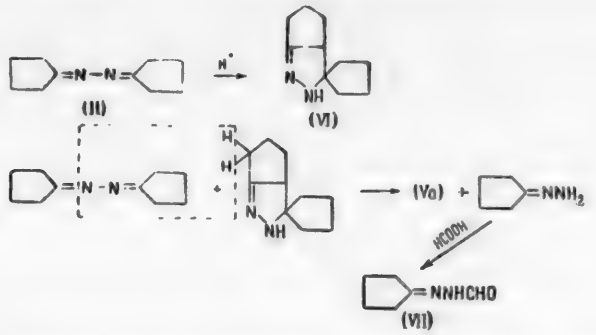


(Vb)

Evidently the pyrazoline (VI), formed initially from cyclopentanone azine (II), under the action of the acidic reagent, enters into a crotonic type condensation with a second molecule of the azine (in a manner analogous to

*The spectra were recorded by N. B. Kupletskaia on an SF-4 spectrophotometer. The solvent was methyl alcohol.
**In a previous paper [9] it was erroneously stated that the reaction occurred with acetic acid.

that taking place with aldimines [10]), whereupon, in the case of formic acid the hydrazone formylates.



On attempting to decompose the pyrazoline (V) by the method of Kirschner we did not succeed in obtaining the corresponding cyclopropane hydrocarbon, having a double carbon-carbon bond, conjugated with the four-membered ring (much resinification occurred).

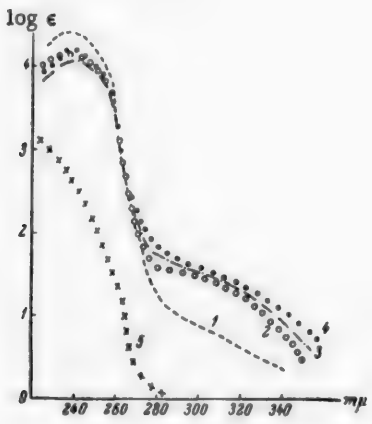


Fig. 1. Absorption spectra of 1-acyl--3,5,5-trimethylpyrazolines. 1) 1-acetyl-(λ_{max} 236 mμ, logε 4.403); 2) 1-propionyl-(λ_{max} 239 mμ, log ε 4.135); 3) 1-butyryl- (λ_{max} 239 mμ, log ε 4.117); 4) 1-isovaleryl-(λ_{max} 239 mμ, log ε 4.134); 5) sym-dibenzoylhydrazine.

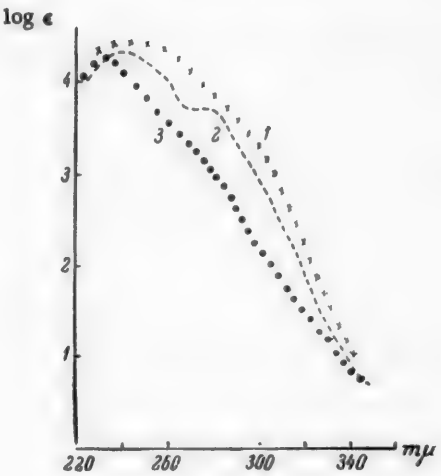


Fig. 2. Absorption spectra of 1-benzoylpyrazolines. 1) 1-benzoyl-3,5,5--trimethylpyrazoline (λ_{max} 247 mμ, log ε 4.348); 2) 1-benzoyl-4-ethyl--5-propylpyrazoline (λ_{max} 235-238 mμ, log ε 4.255); 3) sym-dibenzoylpyrazoline (λ_{max} 232 mμ, log ε 4.279).

It is interesting that the crystals of substance (V), the molecule of which is clearly symmetrical, possess a strong piezoelectric effect, almost equal to that of quartz (according to data provided by V. A. Koptsik*).

While investigating the action of various acidic reagents on azines we noticed that cyclohexanone azine reacts vigorously with phosphorus tribromide. We tried to moderate the conditions and carried out the reaction in dioxan. Unexpectedly, as well as the octahydrocarbazole [11], β,β'-dibromodiethyl ether (bromex) was obtained in good yield (calculated on the phosphorus tribromide), being formed by opening of the dioxan ring. Without the addition of cyclohexanone azine or with the addition of other bases, we either failed to obtain Bromex from dioxan by the action of phosphorus tribromide, or the yield was very small. Phosphorus trichloride under these con-

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ditions does not cyclize cyclohexanone azine and does not give Chlorex.

EXPERIMENTAL

Cyclopentanone azine (II). To 168 g (2 moles) cyclopentanone and 100 ml ethyl alcohol, with external cooling (0-2° in the mixture) and stirring, 52 g (1 mole) of 96% hydrazine hydrate was added dropwise. After 1-2 hours 150 g potash was added and the mixture extracted 3 times with ether. After drying over potash and distilling of the solvent the material was redistilled in vacuo. 131 g (80%) of the azine (II) was obtained. On standing, the azine crystallized in the form of white, needle-shaped crystals with m.p. 24-24.5°.

B.p. 118.5° (14 mm), $n^{20}D$ 1.5222, d^{20}_4 1.0122, MR_D 49.51; calc. 49.69.

Literature data: b.p. 130-132° (22 mm), m.p. 25° [12].

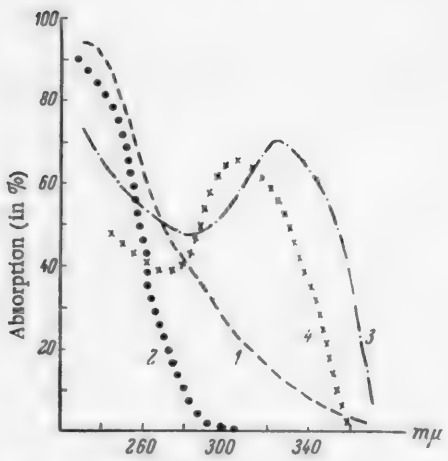

Fig. 3. Absorption spectra of cyclopentanone azine and its transformation products.
1) cyclopentanone azine; 2) cyclopentanone formylhydrazone; 3) 3,4-trimethylene-5,5--pentamethylenepyrazoline (λ_{max} 324 mμ); 4) substance (V) with m.p. 140° (λ_{max} 304 mμ).

Methylisopropylketazine. A mixture of 72.5 g (0.85 mole) methylisopropylketone, 21.3 g (0.43 mole) 96% hydrazine hydrate and 20 ml alcohol was boiled under reflux for 10 hours. 25 g potash was then added and the mixture extracted twice with ether. After drying over magnesium sulfate and redistilling twice, in vacuo, 50 g (70%) of methylisopropylketazine was obtained.

B.p. 78-79° (16 mm), $n^{20}D$ 1.4519, d_{20} 0.8728, MR_D 51.46; calc. 51.18.

Found %: N 16.69, 16.77. $C_{10}H_{20}N_2$. Calculated %: N 16.65.

Literature data: b.p. 165° [13].

The action of benzoylating agents on acetone azine. To 22 g acetone azine 24 ml benzoyl chloride was added dropwise. The temperature of the reaction mixture rose exothermically to 100-110° and considerable resinification took place. The mass, which crystallized on cooling, was extracted with hot benzene. 15.3 g (93.8%) of N,N'-dibenzoylhydrazine, with m.p. 237-238° [14], was isolated from the benzene solution.

Found %: N 11.61, 11.66. $C_{14}H_{12}O_2N_2$. Calculated %: N 11.66.

Absorption spectrum (in alcohol): λ_{max} 232 mμ, log ε 4.279.

When the reaction was carried out with careful exclusion of moisture, evolution of hydrogen chloride took place. On vacuum distillation benzoic acid and 1-benzoyl-3,5,5-trimethylpyrazoline (I) was isolated. Yield 12.4%.

B.p. 145-147° (6 mm), m.p. 92-93° [8]. Absorption spectrum (in alcohol): λ_{max} 247 mμ, log ε 4.348.

Found %: C 71.87, 71.96; H 7.67, 7.72. $C_{13}H_{16}ON_2$. Calculated %: C 72.19, H 7.45.

Similarly, to 11.2 g acetone azine 22.6 g benzoic anhydride in 25 ml anhydrous benzene was added, with stirring. After 1 hour the solvent was distilled off and from a fraction collected (b.p. 51-93°) acetone semicarbazone, with m.p. 185-186°, was obtained by the action of semicarbazide. The residue in the flask was washed three times with hot 2 N sodium hydroxide solution, yielding 2.2 g benzoic acid (m.p. 121-122°, giving no melting point depression with a pure sample) and 18 g (75%) N,N'-dibenzoylhydrazine with m.p. 234-238°, λ_{max} 231-232 mμ.

The reaction of acetone azine with acetyl chloride. 11.2 g of the freshly redistilled azine was added dropwise, with continuous stirring and external cooling, to 50 ml of freshly redistilled acetyl chloride. After 2.5 hours, without cessation of stirring, the mixture was heated to 75° and after 20 minutes the temperature was raised to 100°. The excess acetyl chloride was then distilled off; the residual oil crystallized out. On recrystallizing from petroleum

ether, colorless, cubic crystals of 1-acetyl-3,5,5-trimethylpyrazoline (IV), were obtained. Yield 7.4 g (49%), m.p. 44.5° [4]. No depression of melting point was given with a sample obtained by the action of excess acetic anhydride on 3,5,5-trimethylpyrazoline at −5°. Yield 83%, m.p. 44-45°, λ_{max} 236 mμ, log ε 4.403.

The reaction of butyraldazine with benzoyl chloride. 18 ml benzoyl chloride was added to 14 g butyraldazine. After exothermal reaction had ceased the mixture was heated on the water-bath under reflux for 1.5 hours, treated with 100 ml water and extracted with 50 ml ether. White crystals of N,N'-dibenzoylhydrazine, with m.p. 236-238°, then separated out. Yield 2.7 g (22.5%), λ_{max} 232 mμ. From the ethereal extract, after drying over potash and redistilling, 3 g (16%) 1-benzoyl-4-ethylpropylpyrazoline (III) was obtained.

B.p. 210-215° (17 mm), $n^{20}D$ 1.5690 [8].

Absorption spectrum: λ_{max} 238 mμ, log ε 4.255.

The reaction of methylisopropylketazine with benzoyl chloride. 5.1 g of the azine of methylisopropylketone was added dropwise, with shaking, to 8.4 g of freshly redistilled benzoyl chloride. An exothermal reaction and partial resinification occurred. The resulting mass was poured into 150 ml of 2 N sodium hydroxide solution. The crystals of dibenzoylhydrazine deposited were washed with sodium hydroxide solution and hot water. Yield: 5.3 g (74%), m.p. 232-236°. 3.8 g benzoic acid was isolated from the wash water after acidification. Attempts to carry out cyclization of the azine of methylisopropylketone with formic or oxalic acids were not successful (either extensive resinification occurred or the azine was recovered unchanged).

The reaction of cyclopentanone azine (II) with acyl halides. 9.2 g acetyl chloride was added in small portions to a solution containing 8.2 g of the azine (II) in 50 ml ether, with external cooling (solution temperature 5°) and stirring. The precipitated N,N'-diacetylhydrazine was filtered off and dried in a vacuum desiccator over phosphoric anhydride. Yield 4.2 g (72%) m.p. 139-140° [15].

Similarly, from 8.2 g of the same azine and 15 ml benzoyl chloride in 50 ml benzene (without cooling), 23 g of a brown resinous mass was obtained, from which, after extraction with 5 N aqueous sodium hydroxide, followed by acidification with hydrochloric acid and recrystallization from absolutealcohol, 2.5 g (21%) of N,N'--dibenzoylhydrazine, m.p. 232-234° was obtained.

The reaction of cyclopentanone azine (II) with oxalic acid. 32.8 g of the azine (II) was mixed with 27 g of carefully ground, anhydrous oxalic acid and allowed to stand for three days at room temperature. The viscous mass was decomposed by the addition of 500 ml of 2N aqueous potassium hydroxide solution. The deposited crystals of substance (V), after separation, were washed with water, dried in a vacuum desiccator and recrystallized 6 times from benzene; m.p. 140°. Yield 26 g (66%).

Found %: C 77.98, 78.09; H 9.70, 9.64; N 12.28, 12.39. $C_{15}H_{22}N_2$. Calculated %: C 78.26; H 9.54; N 12.18.

The substance is soluble in dilute hydrochloric acid and can be recovered by addition of alkali. Darkens on prolonged standing in air. Decomposes under the action of oxidizing agents, with evolution of nitrogen.

Picrate, m.p. 176.5° (from alcohol).

Found %: N 15.32, 15.39. $C_{21}H_{25}O_2N_5$. Calculated %: N 15.24.

Benzoyl derivative m.p. 181° (from methyl alcohol).

Found %: C 79.33, 79.21; H 7.80, 7.91; N 8.44, 8.59. Calculated %: C 79.00; H 7.83; N 8.38.

If the reaction between the azine (II) and oxalic acid is carried out at 50° for 1 hour, after treatment with alkali and distillation of the benzene extract, 55% of unchanged azine (II) and 30% substance (V), b.p. 180° (6 mm), m.p. 140° (from benzene) are obtained.

The reaction of cyclopentanone azine (II) with formic acid. 32.8 g of the azine (II) was mixed with 13.8 g of anhydrous formic acid. After 6 hours (at room temperature) the viscous, partially crystallized oil was decomposed with 300 ml of 2N sodium hydroxide solution. The crystals deposited were separated, by crystallizing twice from benzene, into substance (V), m.p. 139-140°, identical with that described in the previous experiment (giving no mixed melting point depression), and cyclopentanone formylhydrazone (VII), m.p. 125.5-126°.

Found %: C 57.24, 57.40; H 8.05, 8.12; N 22.36, 22.48. $C_6H_{10}ON_2$. Calculated %: C 57.15; H 7.99; N 22.22.

This same substance, with m.p. 127° (from benzene), giving no mixed melting point depression with that described above, was obtained by refluxing equivalent quantities of cyclopentanone and formylhydrazine, in alcoholic solution for 2 hours.

The reaction of dioxan with phosphorus tribromide in the presence of cyclopentanone azine. A mixture of 39.2 g cyclopentanone azine, 55 g phosphorus tribromide and 70 ml dioxan was heated to boiling for 2 hours. At the end of the reaction the reaction mixture was poured into water and the heavy layer that separated washed with sodium carbonate, dilute hydrochloric acid, and water; dried over calcium chloride and redistilled in vacuo. 32.7 g (69%) of β,β'-dibromodiethyl ether was obtained.

B.p. 123.5° (47 mm), $n^{20}D$ 1.5125, d^{20}_4 1.8452, MR_D 37.76; calc. 37.84.

Found %: C 20.88, 21.00; H 3.64, 3.61. $C_4H_8OBr_2$. Calculated %: C 20.68; H 3.45.

Literature data: b.p. 115° (32 mm); $n^{20}D$ 1.5131, d^{20}_4 1.8222 [16].

In addition 12 g (30%) of octahydrocarbazole, b.p. 158-166° (13-14 mm), m.p. 87° [11], was isolated.

No Bromex was obtained by boiling dioxan with phosphorus tribromide for 2 hours. In the presence of pyridine the yield of Bromex was 34%; when triethylamine was used the yield fell to nil. Phosphorus trichloride under analogous conditions did not bring about the formation of Chlorex.

SUMMARY

1. The action of acyl halides on azines has been investigated. It was found that, depending on the conditions and the structure of the azine, the latter either broke down with the formation of the sym-diacylhydrazine, or cyclized to the 1-acylpyrazoline.

2. The structure of the substance formed by the action of acidic reagents on cyclopentanone azine has been investigated.

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DERIVATIVES OF HEXAMETHYLENIMINE

III. SUBSTITUTED N-BENZYLHEXAMETHYLENIMINES

G. S. Kolesnikov and L. I. Shcherbo

The synthesis of aliphatic N-substituted hexamethylenimine derivatives was described previously [1]. Continuing our investigation of the synthesis of hexamethylenimine derivatives, we undertook the synthesis of substituted N-benzylhexamethylenimines, which are hexamethylenimine derivatives containing an aliphatic-aromatic substituent on the nitrogen atom. These compounds were prepared by reacting hexamethylenimine with benzyl halides, containing substituents in the nucleus; we chose fluorine, chlorine and bromine as substituents.

$$(CH_2)_6NH + ArCH_2X \rightarrow (CH_2)_6NCH_2Ar + HX$$

The hydrogen halide formed was bound with hexamethylenimine, of which a sufficient excess was used to combine with all the hydrogen halide formed [1, 2]. The synthesis was carried out by the method described previously [1]. The substituted N-benzylhexamethylenimines were characterized as their picrates. The results obtained are given in the table.

Substituted N-benzylhexamethylenimines with the General Formula $(CH_2)_6NCH_2Ar$

CH_2Ar	Yield (in %)	Boiling point (pressure in mm)	d_{20}^{20}	n_D^{25}
Benzyl	77	145—146° (3)	0.9657	1.5280
o-Fluorobenzyl	50	138—141 (3—4)	1.0340	1.5158
o-Chlorobenzyl	42	136—139 (5)	1.0950	1.5425
m-Chlorobenzyl	47	149—150 (8)	1.0740	1.5104
p-Fluorobenzyl	51	135—136 (15)	1.0430	1.5122
p-Chlorobenzyl	50	162—163 (11—12)	1.0750	1.5109
p-Bromobenzyl	51.5	160—162 (3—4)	1.2640	1.5580

EXPERIMENTAL

N-Benzylhexamethylenimine. From 157 g of hexamethylenimine and 100 g of benzyl chloride in 150 ml of benzene we obtained 101 g of N-benzylhexamethylenimine.

Found: M 190.5; 189.1. $C_{13}H_{19}N$. Calculated: M 189.3.

Picrate, m.p. 145-147° (from alcohol).

Found %: N 13.31; 13.13. $C_{19}H_{22}O_7N_4$. Calculated %: N 13.39.

N-o-Fluorobenzylhexamethylenimine. o-Toluidine was converted, via the diazonium fluoborate, into o-fluorotoluene in 41% yield and the latter had b.p. 112-116°. Bromination at 80-110° converted the o-fluorotoluene into o-fluorobenzyl bromide; the yield was 60% and the b.p. 195-200°. From 30 g of hexamethylenimine and 30 g of o-fluorobenzyl bromide in 50 ml of benzene we obtained 22 g of N-o-fluorobenzylhexamethylenimine.

Found: M 211.8, 207.2. $C_{13}H_{18}NF$. Calculated: M 207.15.

Picrate, m.p. 135-136° (from alcohol).

Found %: N 12.65; 12.64. $C_{19}H_{21}O_7N_4F$. Calculated %: N 12.84.

N-o-Chlorobenzylhexamethylenimine. o-Toluidine was converted via the diazo compound into o-chlorotoluene in 56% yield and the latter had b.p. 156-159°. Bromination at 110° yielded o-chlorobenzyl bromide; the yield was 67% and the b.p. 112-114° at 10 mm. From 56 g of hexamethylenimine and 50 g of o-chlorobenzyl bromide in 100 ml of benzene we obtained 25.5 g of N-o-chlorobenzylhexamethylenimine.

Found: M 221.0; 217.0. $C_{13}H_{18}NCl$. Calculated: M 223.6.

Picrate, m.p. 137-139° (from alcohol).

Found %: N 12.53; 12.78. $C_{19}H_{21}O_7N_4Cl$. Calculated %: N 12.37.

N-m-Chlorobenzylhexamethylenimine. From 58 g of hexamethylenimine and 46 g of m-chlorobenzyl chloride in 100 ml of benzene we obtained 30 g of N-m-chlorobenzylhexamethylenimine.

Found: M 214.0; 216.8. $C_{13}H_{18}NCl$. Calculated: M 223.6.

Picrate, m.p. 152-154° (from alcohol).

Found %: N 12.37, 12.53. $C_{19}H_{21}O_7N_4Cl$. Calculated %: N 12.37.

N-p-Fluorobenzylhexamethylenimine. p-Toluidine was converted via the diazonium fluoborate into p-fluorotoluene in 25.8% yield and the latter had b.p. 114-116°. Bromination of p-fluorotoluene at 80-110° yielded p-fluorobenzyl bromide; the yield was 75.6% and the b.p. 195-200°. From 63 g of hexamethylenimine and 60 g of p-fluorobenzyl bromide in 100 ml of benzene we obtained 45 g of N-p-fluorobenzylhexamethylenimine.

Found: M 203.9, 201.2. $C_{13}H_{18}NF$. Calculated: M 207.15.

Picrate, m.p. 152-154° (from alcohol).

Found %: N 13.04, 13.01. $C_{19}H_{21}O_7N_4F$. Calculated %: N 12.84.

N-p-Chlorobenzylhexamethylenimine. From 76 g of hexamethylenimine and 60 g of p-chlorobenzyl chloride in 150 ml of benzene we obtained 48.1 g of N-p-chlorobenzylhexamethylenimine.

Found: M 217.0, 218.1. $C_{13}H_{18}NCl$. Calculated: M 223.6.

Picrate, m.p. 136-137° (from alcohol).

Found %: N 12.29, 12.05. $C_{19}H_{21}O_7N_4Cl$. Calculated %: N 12.37.

N-p-Bromobenzylhexamethylenimine. By bromination at 120°, p-bromotoluene was converted into p-bromobenzyl bromide; the yield was 70.5%. From 60 g of hexamethylenimine and 77 g of p-bromobenzyl bromide in 100 ml of benzene we obtained 42.6 g of N-p-bromobenzylhexamethylenimine.

Found: M 274.2, 267.1. $C_{13}H_{18}NBr$. Calculated: M 268.5.

Picrate, m.p. 153-155° (from alcohol).

Found %: N 11.26, 11.24. $C_{19}H_{21}O_7N_4Br$. Calculated %: N 11.27.

SUMMARY

We prepared 7 substituted N-benzylhexamethylenimines, 6 of which are described for the first time.

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SYNTHESIS OF SOME AMINOALKYL ETHERS WITH CHOLINOLYTIC PROPERTIES

S. G. Kuznetsov and Z. I. Bobysheva

In searching for cholinolytic preparations, we decided to synthesize aminoalkyl ethers, similar in chemical structure to active cholinolytic substances in the aminoalkyl ester class. Of these, the diethylaminoethyl (I) and dimethylaminoethyl (II) esters are of particular interest, the former is known in American pharmacological literature under the symbol WIN 5606.

$(C_6H_5)_2C(OH)CO{-}O{-}CH_2CH_2N(C_2H_5)_2$ (I) $(C_6H_5)_2C(OH)CO{-}O{-}CH_2CH_2N(CH_3)_2$ (II)

$(C_6H_5)_2C(OH)CH_2{-}O{-}CH_2CH_2N(C_2H_5)_2$ (III) $(C_6H_5)_2C(OH)CH_2{-}O{-}CH_2CH_2N(CH_3)_2$ (IV)

It seemed interesting to synthesize the two aminoalkyl ethers (III) and (IV), which are analogous to the two esters mentioned above. The substitution of the CO group in these compounds by a methylene group must substantially affect their physical and chemical properties, in particular, polarity, solubility, basicity and stability to hydrolysis. It was natural to expect that changes in the physicochemical properties would also affect the cholinolytic activities of the compounds; however, it was difficult to forsee the character and, especially, the degree of change in the properties. The synthesis of these substances and a study of their pharmacological properties could help solve the problem of the relation between chemical structure and physiological activity in this group of compounds.

As the formulas given above show, the compounds we were interested in, (III) and (IV), are partial ethers of unsymmetrical diphenylethylene glycol and diethyl- or dimethylaminoethanol. We first tried using these substances to prepare compounds (III) and (IV).

Danilov [1] prepared unsymmetrical diphenylethylene glycol by reducing diphenylglycolaldehyde. The epichlorohydrin of this glycol was first synthesized by reacting phenylmagnesium bromide with ethyl chloroacetate [2] and then by reacting the chloroacetophenone with phenyllithium [3].

Having prepared the epichlorohydrin of unsymmetrical diphenylethylene glycol, we tried to carry out the following reaction.

$$(C_6H_5)_2C(OH)CH_2Cl + NaOCH_2CH_2N(C_2H_5)_2 \longrightarrow$$
$$\longrightarrow NaCl + (C_6H_5)_2C(OH)CH_2{-}O{-}CH_2CH_2N(C_2H_5)_2$$

However, the reaction did not proceed in the required direction as under the effect of alkaline agents, such as sodium β-diethylaminoethylate, in particular, this epichlorohydrin was very readily converted to unsymmetrical diphenylethylene oxide.

We synthesized the required aminoalkyl ethers in the following way:

$$ClCH_2COOC_2H_5 + NaOCH_2CH_2N(R)_2 \rightarrow C_2H_5OCOCH_2{-}O{-}CH_2CH_2N(R)_2 \rightarrow$$
$$\xrightarrow{2C_6H_5Li} (C_6H_5)_2C(OH)CH_2{-}O{-}CH_2CH_2N(R)_2$$
$$R = CH_3,\ C_2H_5$$

Ethyl chloracetate reacted with sodium β-diethylaminoethylate in benzene solution to give a 20-22% yield of ethyl β-diethylaminoethoxyacetate and, in addition, a substance with a higher boiling point which was, apparently,

the β-diethylaminoethyl ester of β-diethylaminoethoxyacetic acid. The formation of this substance may be explained by the side reaction of transesterification of ethyl chloroacetate and ethyl β-diethylaminoethoxyacetate. Ethyl chloroacetate also reacted with sodium β-dimethylaminoethylate in a similar way.

The second state of the synthesis – the reaction of the substituted acetate with phenyllithium – was carried out under the usual conditions for organolithium synthesis, namely, in an ether solution, without moisture, in an atmosphere of nitrogen and with cooling. The aminoalkyl ethers (III) and (IV) obtained by this reaction were purified by high vacuum distillation, then converted into hydrochlorides and recrystallized in this form. The yield of 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 (III) was 70% and that of 1,1-diphenyl-2-(β-dimethylaminoethoxy)-ethanol-1 (IV) was 56%.

We tried to prepare some derivatives of these aminoalkyl ethers. Heating (IV) with ethyl chloride in an acetone solution gave a 53% yield of the corresponding chloroethylate (V).

$$(C_6H_5)_2C(OH)CH_2—O—CH_2CH_2N(CH_3)_2(C_2H_5)Cl$$
(V)

This compound is interesting in that its chemical structure is analogous to the very active cholinolytic substance – lachesin (VI) – which is well known abroad.

$$(C_6H_5)_2C(OH)CO—O—CH_2CH_2N(CH_3)_2(C_2H_5)Cl$$
(VI)

We also tried to prepare some derivatives of the aminoalkyl ethers (III) and (IV), using the hydroxyl groups in their molecules, and in particular, their chloro and acetyl derivatives. However, either the reaction did not proceed, as was the case, for example, when acetic anhydride or acetyl chloride were used, or proceeded with the elimination of a water molecule and the formation of the corresponding unsaturated compound, as was the case for example, when 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 (III was treated with thionyl chloride. In this case a 70% yield of 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethylene (VII) was obtained and its structure was confirmed by a quantitative determination of the double bond and analysis for nitrogen and chlorine content (of the hydrochloride).

$$(C_6H_5)_2C(OH)CH_2—O—CH_2CH_2N(C_2H_5)_2 \xrightarrow{SOCl_2}$$
(III)

$$\longrightarrow (C_6H_5)_2C{=}CH—O—CH_2CH_2N(C_2H_5)_2 + H_2O$$
(VII)

The aminoalkyl ethers (III), (IV), (V) and (VII) obtained were investigated pharmacologically and as a result it was established that these compounds have a definite cholinolytic activity, but to a considerably lesser degree than the aminoalkyl esters which correspond to them. The most active was a quaternary ammonium derivative of ether (V) and the least active was the unsaturated compound (VII).

One should add that after finishing this work, the report by Parkes [4] appeared in the literature giving the results of the pharmacological investigation of a series of aminoalkyl thioethers and ethers and the two ethers, (III) and (IV), obtained by us, are mentioned among them; however, the author does not indicate by what method and by whom and when these compounds were prepared. No information has as yet been published in the chemical literature on the substances synthesized by us.

EXPERIMENTAL

Ethyl β-diethylaminoethoxyacetate. 11.5 g of sodium was dissolved by heating in 64.3 g of β-diethylaminoethanol. The cooled reaction mixture was diluted with 25 ml of dry benzene and then a solution of 61.25 g of ethyl chloroacetate in 25 ml of benzene wasadded to it at 10-15°. The mixture was kept at room temperature for 2 hours and then at 40° for 1 hour. The whole process was carried out in an atmosphere of hydrogen. Carbon dioxide was passed into the reaction mixture to decompose the remaining alcoholate and then a sufficient amount of water was added to dissolve the precipitate of sodium chloride completely. The benzene layer was separated and the aqueous layer saturated with potassium carbonate and extracted with benzene. The combined benzene extracts were dried with potassium carbonate, the benzene distilled off and the residue vacuum distilled. Three fractions were obtained:

1st fraction – unreacted β-diethylaminoethanol with b.p. 42° (2 mm), 15.9 g; 2nd fraction – ethyl β-diethylaminoethoxyacetate with b.p. 85-86° (2 mm), 22.9 g and a 3rd fraction – apparently, the β-diethylaminoethyl ester of β-diethylaminoethoxyacetic acid with b.p. 128° (2 mm), 3.2 g. A second distillation of the 2nd fraction gave 13.2 g of ethyl β-diethylaminoethoxyacetate. It was a colorless, mobile liquid with the characteristic smell of aliphatic amines. It was readily soluble in water and most organic solvents.

B.p. 79-81° at 2 mm, $n^{20}D$ 1.4339, d^{20}_4 0.9566, MR_D 55.35; calc. 55.62.

Found %: N 6.78, 6.86. $C_{10}H_{21}NO_3$. Calculated %: N 6.89.

Ethyl β-dimethylaminoethoxyacetate was prepared similarly from 8.7 g of sodium, 72.6 g of β-dimethylaminoethanol and 46.5 g of ethyl chloroacetate.

B.p. 75-78° at 2 mm, $n^{20}D$ 1.4285, d^{20}_4 0.9801, MR_D 46.32, calc. 46.38.

Found %: N 7.85, 7.96. $C_8H_{17}NO_3$. Calculated %: N 8.00.

1,1-Diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 (III). A solution of phenyllithium, prepared in the usual way from 2.3 g of lithium and 23.6 g of bromobenzene in 100 ml of absolute ether, was treated at about 0° with a cooled solution of 10.1 g of ethyl β-diethylaminoethoxyacetate in 60 ml of ether. After standing at room temperature for 15-20 hours, the reaction mixture was decomposed with ice water, the ether layer separated and the aqueous layer extracted with ether. The combined ether extracts were treated with dilute hydrochloric acid. The acid aqueous extract was made alkaline with potassium carbonate. Free 1,1-diphenyl-2-(β-diethylaminoethoxy)--ethanol-1 precipitated in the form of an oily liquid and was extracted with ether. After being dried with potassium carbonate, the ether was distilled off and the residue distilled in high vacuum. We collected a fraction with b.p. 130° at 0.006 mm, which crystallized on standing. The yield was 10.9 g (70%). The colorless crystals (from petroleum ether) with m.p. 55-57° were readily soluble in organic solvents and difficultly soluble in water.

Found %: N 4.43, 4.25; OH 5.92, 5.76. $C_{20}H_{27}O_2N$. Calculated %: N 4.47; OH 5.42.

The hydrochloride of 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 formed colorless crystals (from a mixture of anhydrous alcohol and ether) with m.p. 181-182°.

Found %: Cl 9.76, 10.01. $C_{20}H_{28}O_2NCl$. Calculated %: C 10.13.

1,1-Diphenyl-2-(β-dimethylaminoethoxy)-ethanol-1 (IV) was prepared similarly from 3.5 g of ethyl β-dimethylaminoethoxyacetate and a solution of phenyllithium, prepared from 1 g of lithium and 11 g of bromobenzene. The yield was 3.2 g (56%). The thick oily liquid had b.p. 145° at 0.03 mm.

The hydrochloride of 1,1-diphenyl-2-(β-dimethylaminoethoxy)-ethanol-1 formed a colorless crystalline powder with m.p. 169-170° (from a mixture of alcohol and ether).

Found %: Cl 10.73, 10.89; N 4.19, 4.44. $C_{18}H_{24}O_2NCl$. Calculated %: Cl 11.02; N 4.35.

Chloroethylate of 1,1-diphenyl-2-(β-dimethylaminoethoxy)-ethanol-1 (V). This was prepared by heating 1.72 g of (IV) with 8.5 ml of acetone and 6 ml of ethyl chloride for 6 hours at 65-70° in a sealed tube. The colorless crystals (from a mixture of alcohol and acetone) had m.p. 140-142°. The yield was 0.95 g (44%).

Found %: Cl 9.73, 9.86; N 4.10. $C_{20}H_{28}O_2NCl$. Calculated %: Cl 10.13; N 4.00.

The hydrochloride of 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethylene. To a solution of 3.5 g of 1,1-diphenyl--2-(β-diethylaminoethoxy)-ethanol-1 hydrochloride in 20 ml of chloroform was added 2 ml of thionyl chloride, diluted with 5 ml of chloroform and the mixture heated at 40-45° for 2 hours. After removal of the solvent in vacuum, the residue was recrystallized from a mixture of alcohol and ether. The colorless crystals had m.p. 142-144°. The yield was 2.3 g (70%).

Found %: Cl 10.56, 10.76. Bromine number 45.9, 43.9. $C_{20}H_{26}ONCl$. Calculated %: Cl 10.68. Bromine number 48.1.

SUMMARY

1. By reacting the ethyl chloroacetate with sodium β-dimethylaminoethylate and with sodium β-diethylaminoethylate we synthesized ethyl β-dimethylaminoethoxyacetate and ethyl β-diethylaminoethoxyacetate.

2. Reaction of phenyllithium with these esters gave 1,1-diphenyl-2-(β-dimethylaminoethoxy)-ethanol-1 and 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1. The hydrochlorides of both these compounds and the chloroethylate of 1,1-diphenyl-2-(β-dimethylaminoethoxy)-ethanol-1 were prepared.

3. Dehydration of 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 by treatment with thionyl chloride gave 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethylene.

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INVESTIGATION OF THE HYDROGEN BOND IN SOME CHOLINOLYTIC SUBSTANCES USING INFRARED ABSORPTION SPECTRA

S. G. Kuznetsov and V. N. Nikitin

The considerable effect that a hydrogen bond has on the physical and chemical properties of a substance is well known. Some also believe that the formation of a hydrogen bond may play an important part in the mechanism of physiological activity of a series of substances, among them medicinal, selectively toxic and other materials [1-4]. Such a hypothesis is also put forward in relation to cholinolytic substances like atropine and its synthetic analogs, which contain a hydroxyl group in the molecule. It is also considered that the hydrogen of the hydroxyl group of the cholinolytic substance participates in a donor-acceptor reaction with some electron donor (atom) which corresponds to the biochemical structure of the organism [5].

Of the synthetic analogs of atropine, β-diethylaminoethyl benzilate (II), mentioned in American pharmacological literature under the symbol WIN 5606, is of considerable interest. Its analog (I), which does not contain a hydroxyl and is known abroad as trasentine and here as spasmolitin, is considerably less active as a cholinolytic.

$$(C_6H_5)_2CHCO-O-CH_2CH_2N(C_2H_5)_2 \quad (I)$$

$$(C_6H_5)_2C(OH)CO-O-CH_2CH_2N(C_2H_5)_2 \quad (II)$$

However, among the group of cholinolytic substances containing a hydroxyl there are some that have a low cholinolytic activity. According to the data given by Parkes [6] a particular one of these is 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 (III), which differs from the active compound (II) in that the CO group in the latter is replaced by a CH_2 group.

$$(C_6H_5)_2C(OH)CH_2-O-CH_2CH_2N(C_2H_5)_2 \quad (III)$$

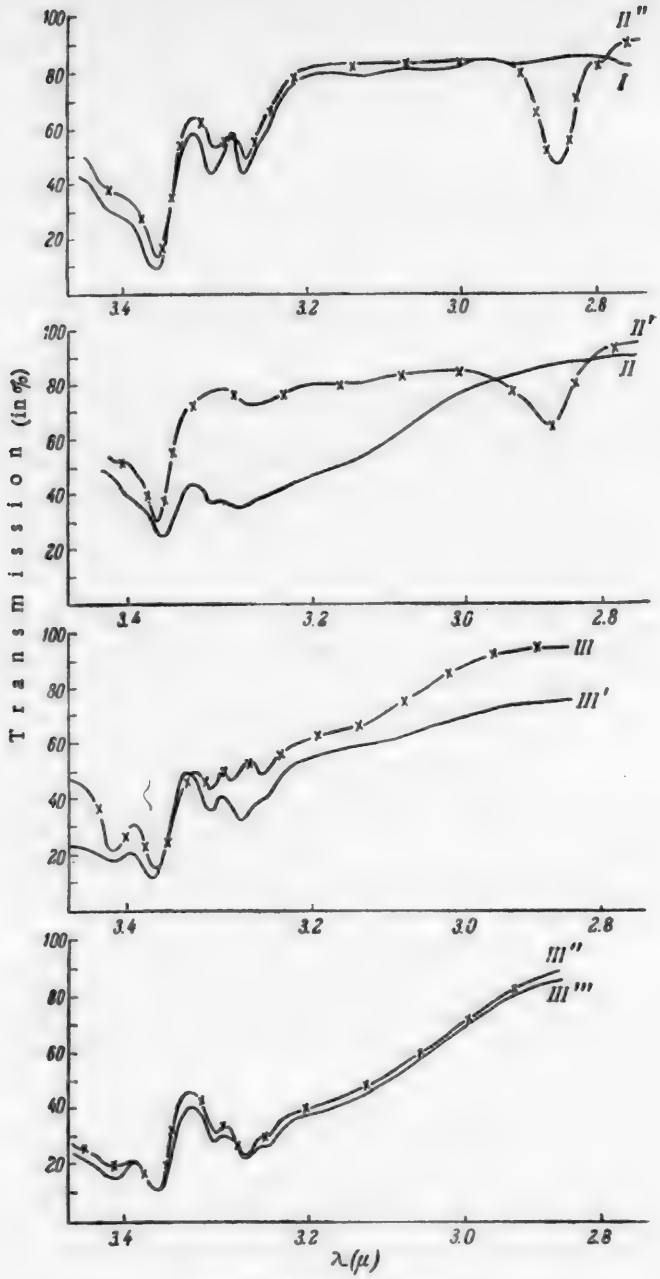
It seemed interesting to us to investigate the infrared absorption spectra of these three compounds, the first being used only for a comparison. One might expect that the difference in the physiological activity of substances (II) and (III) was related to the difference in the properties of their hydroxyl groups, which would also be reflected in their oscillation spectra.

Substances (I) and (II) were prepared by the methods described in the literature [7, 8]. As the synthesis and properties of substance (III) are not described in the literature, we developed a method for its preparation [9].

The substances were purified in the form of the hydrochlorides by crystallization and as the free bases by distillation in high vacuum and crystallization from petroleum ether until constant melting points were obtained. The melting points of the hydrochlorides of the substances investigated and the bases themselves are given below.

Substances (I), (II) and (III) were investigated in the form of free bases. The infrared absorption spectra were plotted on an IKS-146 infrared spectrometer with an LiF prism in the range 2.7-3.5 μ for the pure substances and their solutions in CCl_4. The data obtained are shown in the figure.

Substance (I)(Curve I) has no absorption in the region 3.2-2.8 μ, which agrees with the absence of an OH group in its molecule. In the crystalline state substance (II) has a broad absorption band in the region 3.2-3.0 μ which indicates the presence of a hydrogen bond in it (Curve II). However, when substance (II) is in a molten state (~60°) the broad band in this region disappears and simultaneously a narrow band appears at 2.870 μ which characterizes the oscillation of a free hydroxyl (Curve II'). An analogous picture was observed for a solution of substance (II) in CCl_4, where a narrow band of free hydroxyl appears at 2.855 μ (Curve II"). All this indicates the



Infrared absorption spectra.

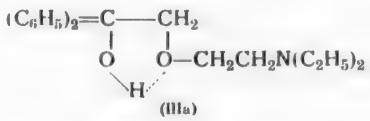
I) $(C_6H_5)_2CHCO-O-CH_2CH_2N(C_2H_5)_2$ solution in CCl_4; (c 0.126 m, d 0.29 mm); II") $(C_6H_5)_2C(OH)CO-O-CH_2CH_2N(C_2H_5)_2$ solution in CCl_4 (c 0.118 m, d 0.29 mm); II and II') $(C_6H_5)_2C(OH)CO-O-CH_2CH_2N(C_2H_5)_2$, at 20 and 60°, respectively (c 1, d 20μ); III and III') $(C_6H_5)_2C(OH)CH_2-O-CH_2CH_2N(C_2H_5)_2$, at 20 and 100°, respectively (c 1, d 20μ); III" and III"') $(C_6H_5)_2C(OH)CH_2-O-CH_2CH_2N(C_2H_5)_2$ solutions in CCl_4 (c 0.122 m, d 0.29 mm and c_1 0.00177 m, d_1 20 mm, respectively; $c \cdot d = c_1 \cdot d_1$).

formation of an intermolecular hydrogen bond in substance (II), which is broken when the substance is liquid or dissolved in CCl_4.

Substance	Melting point	
	hydrochloride	Base
(I)	115-116°	Liquid
(II)	177-178	53-55°
(III)	181-182	55.5-56.5

In the crystalline state substance (III) has a broad absorption band at 3.2-3.0 μ, which corresponds to the OH group in the hydrogen bond (Curve III). When the substance is heated above the melting point (100°) no band appears corresponding to the oscillations of free hydroxyls (Curve III').

Curves III° and III''' characterize the absorption spectra of solutions of substance (III) at 0.122 and 0.00177 M concentrations in vessels 0.29 and 20 mm thick, respectively (the product of concentration and thickness of solution layer is constant). One can see that absorption in the region of 3.2-3.0 μ does not change with the concentration of substance (III). The invariability of the spectra of substance (III) and the absence of a band at 2.87 μ, which characterizes the oscillation of free hydroxyls, indicate that an intramolecular hydrogen bond exists in substance (III) and remains in the melt and in the solution. This bond probably forms with the participation of the ether oxygen by scheme (IIIa).



(IIIa)

The results obtained seem to indicate that of the three substances investigated only substance (II) should have the tendency to form quite stable intermolecular hydrogen bonds with other suitable substances. Substance (I) cannot have this capacity as it lacks a hydroxyl group, while the hydroxyl group in substance (III) is inactive due to the formation of an intramolecular hydrogen bond. It is noticeable that the results obtained agree with the fact that of the substances investigated only substance (II) has a high cholinolytic activity, while substances (I) and (III) have low and approximately equal activities, which confirms, to a certain degree, the hypothesis of the role of the hydroxyl group in the mechanism of cholinolytic activity of the substances of this series.

SUMMARY

1. We investigated the infrared absorption spectra of three cholinolytic substances: β-diethylaminodiphenylethyl acetate, β-diethylaminoethyl benzilate and 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1.

2. It was concluded from the data obtained that the hydroxyl group in diethyl aminoethyl benzilate was capable of forming an intermolecular hydrogen bond and in 1,1-diphenyl-2-(β-diethylaminoethoxy)-ethanol-1 an intramolecular hydrogen bond.

3. A hypothesis was put forward on the relation of cholinolytic activity of these compounds to the capacity of their hydroxyl groups to form intermolecular hydrogen bonds.

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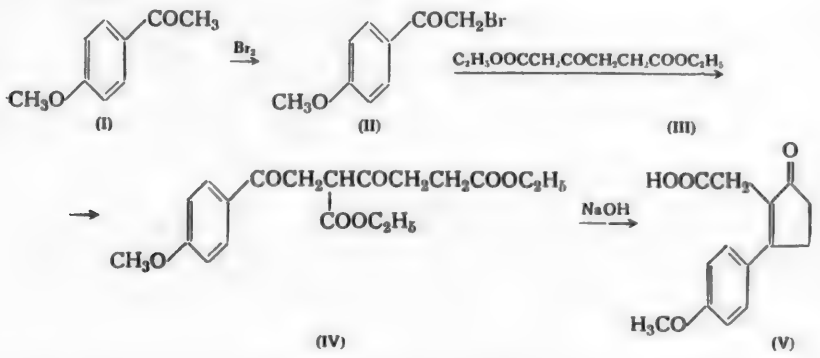
INVESTIGATIONS OF THE SYNTHESIS OF STEROID HORMONE ANALOGS

III. PREPARATION OF 3-(p-METHOXYPHENYL)-Δ^2-CYCLOPENTEN-1-ONE-2-ACETIC ACID

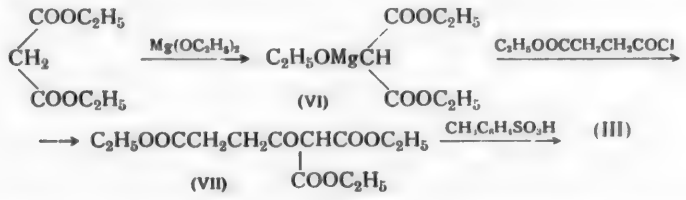
G. S. Grinenko and V. I. Maksimov

3-(p-Methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid (V) was the starting material in our work on the complete synthesis of some analogs of steroid hormones. Robinson [1] was the first to prepare this acid from p--methoxyacetophenone and furfurole, in the form of needles with m.p. 133° (after recrystallization from acetone and benzene). Later, Turner [2] used Robinson's method to prepare acid (V) with the same m.p. 132-133°; he prepared its methyl ester with m.p. 87-89°.

In our work we synthesized acid (V) by another method, based on the process, proposed by Borsche [3] for Δ^2-3-phenylcyclopentenone.

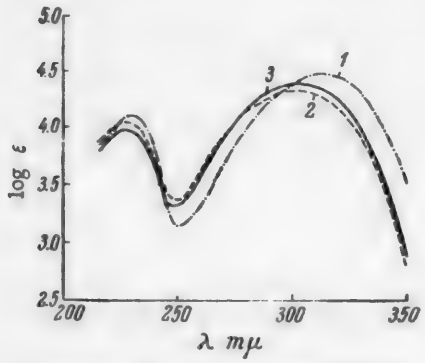


The starting materials were p-methoxy-ω-bromoacetophenone (II) [4] and diethyl β-ketoadipate (III), which was prepared by the method of Riegel and Lilienfeld [5] by acylating the magnesium derivative of diethyl malonate (VI) with the acid chloride of the half ester of succinic acid followed by hydrolysis and decarboxylation of the tricarboxylic ester formed (VII). In contrast to Riegel and Lilienfeld, we prepared ethoxymagnesiomalonic ester (VI) by reacting malonic ester with magnesium alcoholate and not with a suspension of magnesium in alcohol. This decreased the reaction time considerably. We hydrolyzed and decarboxylated the tricarboxylic ester (VII) with p-toluenesulfonic acid and not with naphthalenesulfonic acid.

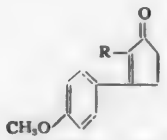


Condensation of diethyl β-ketoadipate (III) with p-methoxy-ω-bromoacetophenone (II) gave a substituted ester of diketoheptanonic acid (IV), which without further purification (as it was converted to the corresponding

furancarboxylic ester when distilled) was heated with a 2% solution of sodium hydroxide. Acid (V), obtained by this method in the form of needles, had m.p. 145.5-146° after recrystallization from water, i.e., 12-13° higher than that reported by Robinson and Turner. Recrystallization from acetone and benzene (as performed by these investigators) did not change its melting point.



Ultraviolet absorption spectra of α,β-unsaturated ketones of the type:



1 — R = H, 2 — R = CH_3, 3 — R = CH_2COOH.

We also prepared acid (V) by Robinson's method; it also had melting point 145.5-146° and did not depress the melting point of the acid prepared by our method.

The methyl ester of the acid we prepared had m.p. 88-89°, which agrees with the literature data. By hydrolyzing it we isolated an acid with m.p. 145.5-146°, while when Turner [2] hydrolyzed a methyl ester with the same melting point, he obtained an acid with m.p. 132-133°.

The ultraviolet spectra of acid (I) and its methyl ester are characteristic of α,β-unsaturated ketones, which have a carbonyl group, double bond and aromatic ring conjugated in the molecule [6], and agree with the spectra of 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one and 3-(p-methoxyphenyl)-2-methyl-Δ^2-cyclopenten-1-one.

These spectroscopic investigations confirmed that the acid we prepared by two methods with m.p. 145.5-146° was actually 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid. Apparently, Robinson and Turner prepared another polymorphous modification which melted at 133°.

EXPERIMENTAL

Diethyl ester of β-ketoadipic acid III [5]. 24.3 g of magnesium turnings, 4 ml of dry carbon tetrachloride and 157 ml (124 g) of anhydrous alcohol were boiled until the evolution of hydrogen ceased (2.5 hours). The preparation of ethoxymagnesiomalonic ester was performed without stirring. The magnesium turnings reacted with the alcohol vapor to form a friable, white precipitate, which was cooled and to which was added dropwise and with stirring 160 g of malonic ester in 300 ml of dry ether, the mixture was then boiled for 1 hour. Then the alcohol and ether were distilled off from the mixture. The remainder of the alcohol was distilled off with benzene. 185 g of β-carbethoxypropionyl chloride, dissolved in 150 ml of dry ether, was added dropwise with stirring to a solution of the ethoxymagnesiomalonic ester in 300 ml of dry ether and the whole boiled for 2 hours. After being cooled, the reaction mixture was hydrolyzed with 600 ml of 5% sulfuric acid. The ether layer was separated and the aqueous layer extracted with ether. The combined ether extracts were dried. The residue after evaporation of the ether was slowly heated up to 200° in the presence of 14 g of p-toluenesulfonic acid monohydrate until the evolution of carbon dioxide ceased. After being cooled, the reaction mixture was dissolved in ether. The ether solution was washed with a cold, concentrated solution of sodium carbonate and dried. The carbonate solution was acidified with 5% hydrochloric acid and extracted with ether. The residue from evaporating this ether solution was decarboxylated as described above. The two fractions, which were insoluble in soda solution, were evaporated down and distilled. We obtained 125.5 g (58%) of diethyl β-ketoadipate (III) with b.p. 122-126° at 0.5 mm ($n^{20}D$ 1.4555).

Found %: C 55.41; H 7.29. $C_{10}H_{16}O_5$. Calculated %: C 55.54; H 7.46.

Ethyl ester of 2-(p-methoxyphenacyl)-3-ketoadipic acid (IV). To 2.3 g of finely divided metallic sodium in 200 ml of dry ether was added 22 g of diethyl β-ketoadipate in 200 ml of dry ether over a period of 30 minutes. The reaction mixture was heated and stirred until the sodium completely dissolved (4 hours). The solution was cooled, 23 g of p-methoxy-ω-bromoacetophenone [4] in 300 ml of dry ether added and the mixture boiled for 6 hours. The reaction mixture was cooled and water added until the sodium bromide dissolved. The ether layer

was separated and the aqueous layer extracted with ether. The combined ether extracts were washed with water and dried with anhydrous sodium sulfate. Evaporation of the ether left 36.2 g (quantitative yield) of ethyl 2-(p--methoxyphenacyl)-3-ketoadipate as a brownish oil, which could be used for intramolecular condensation without purification.

3-(p-Methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid (V). 36.2 g of unpurified ethyl 2-(p-methoxyphenacyl)-3-ketoadipate was boiled with 2000 ml of 2% potassium hydroxide with stirring for 1 hour in a stream of nitrogen. During this time the oily layer dissolved completely. The solution was cooled, 100 g of sodium chloride added and the reaction mixture made slightly acid with hydrochloric acid. The oil which separated was extracted with chloroform. The chloroform extract was washed with water and dried with anhydrous sodium sulfate. Evaporation of the solvent gave 12.5 g of a brown precipitate. After 2 recrystallizations from 1000 ml of water with charcoal, we obtained 7.3 g (29.7%) of 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid with m.p. 145.5-146° as long needles with $\lambda_{max}^{C_2H_5OH}$ 228, 301 mμ, log ε 4.04, 4.33. Recrystallization from acetone and benzene gave 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid with constant melting point. The acid was readily soluble in alcohol, acetone, benzene and chloroform and difficultly soluble in ether, benzine and water.

Found %: C 68.19; H 5.76. $C_{14}H_{14}O_4$. Calculated %: C 68.26; H 5.74.

Methyl ester of 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid. To a solution of 1 g of the acid (V) and 0.26 g of potassium hydroxide in 20 ml of water was added a solution of 0.7 g of silver nitrate in 10 ml of water and the mixture stirred for 10 minutes. A white precipitate of the silver salt precipitated immediately. This was filtered off and washed on the filter with methyl alcohol and then with ether. The precipitate of the silver salt was placed in a flask and boiled under reflux with 2.6 ml of methyl iodide in 30 ml of ether for 1 hour. The yellow precipitate of silver iodide formed was filtered off. The ether solution was washed with 5% alkali solution, then with water, and dried with anhydrous sodium sulfate. Evaporation of the ether yielded 0.85 g of methyl 3-(p--methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetate with m.p. 87-88.5°. After recrystallization from methyl alcohol, the material had m.p. 88-89°. The yield was 80%. $\lambda_{max}^{C_2H_5OH}$ 228, 301 mμ, log ε 4.03, 4.35. The substance was readily soluble in alcohol, ether, benzene and chloroform and difficultly soluble in benzine.

Found %: C 69.16; H 6.25. $C_{15}H_{16}O_4$. Calculated %: C 69.21; H 6.22.

Hydrolysis of methyl 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetate. A solution of 0.3 g of methyl 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetate in 10 ml of 2% potassium hydroxide in methyl alcohol was left to stand at room temperature for 24 hours. The reaction mixture was neutralized with acetic acid. The residue from distillation of the methanol in vacuum was recrystallized from 25 ml of water. We obtained the acid (V) with m.p. 145.5-146°.

SUMMARY

1. Starting with p-methoxy-ω-bromoacetophenone and diethyl β-ketoadipate, we synthesized 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid with m.p. 145.5-146°.

2. When we prepared this acid by Robinson's method, it had the same m.p. 145.5-146°.

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INVESTIGATIONS IN THE FIELD OF ANALOGS OF STEROID HORMONES

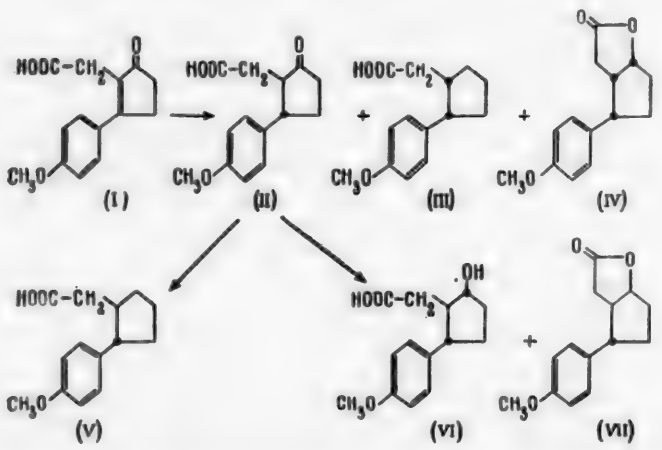
IV. CATALYTIC HYDROGENATION OF 3-(p-METHOXYPHENYL)-Δ^2-CYCLOPENTEN-1-ONE-2--ACETIC ACID

G. S. Grinenko and V. I. Maksimov

During investigations in the field of analogs of steroid hormones, catalytic hydrogenation of the double bond of 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid (I) gave us trans-3-(p-methoxyphenyl)-cyclopentan--1-one-2-acetic acid (II).

The work by Weidlich [1] showed that on reducing a ditertiary double bond of α,β-unsaturated ketones in the presence of a palladium catalyst, a trans-ketone is formed preferentially in an alkaline or neutral medium while a cis-ketone is formed in an acid medium. This observation agrees with the relation between the reaction rate and energy content of the reaction product, established by Zal'kind [2] and Ott [3]. With a rapid rate of hydrogenation (in an acid medium) the isomer mainly formed is that which has a high energy (cis-isomer); as the time of reaction increases (in an alkaline medium) the isomer formed in increasing amount is one with less energy (trans-isomer).

We hydrogenated 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid (I) with palladium on calcium carbonate in alkaline (potassium hydroxide, 10% of the acid's weight) and in neutral solutions under atmospheric pressure. The ditertiary double bond was reduced very slowly under these conditions. The application of slight excess pressure (3-5 atm.) considerably increased the hydrogenation rate. In both cases, absorption of hydrogen ceased after the addition of 1.3 moles of hydrogen. The hydrogenation gave a mixture of three substances; trans--3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid (II), with m.p. 106.5-107.5° (77%), cis-2-(p-methoxyphenyl)-cyclopentane-1-acetic acid (III) with m.p. 73-74° (8.5%) and the lactone of syn-cis-3-(p-methoxyphenyl)--cyclopentan-1-ol-2-acetic acid (IV) with m.p. 67-68° (5.8%).

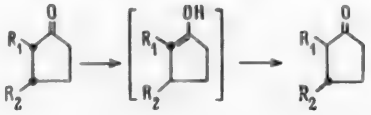


When hydrogenation was stopped after absorption of 1 mole of hydrogen, in addition to the three substances

described above, we isolated the starting keto acid (I). Attempts to further hydrogenate the keto acid (II) isolated under the same conditions (in the presence of a palladium catalyst at 3-5 atm) gave negative results. This indicated that the "perhydrogenation" products (III) and (IV) were formed, not from the saturated keto acid (II), but parallel with it from the unsaturated keto acid (I).

Hoping to obtain another isomer of the saturated keto acid (II), we hydrogenated acid (I) in an acid medium in the presence of palladium on barium sulfate and palladium on charcoal at atmospheric pressure and room temperature. Hydrogen was absorbed very rapidly, without any noticeable slowing down until absorption stopped sharply, after the addition of 3 moles of hydrogen. The only reaction product isolated was cis-acid (III) with m.p. 73-74°. As in the first case, when hydrogenation was stopped after the absorption of 1 mole of hydrogen, a mixture of the starting acid (I) and acid (III) was obtained.

Thus, by hydrogenation we were able to obtain only one stable isomer of keto acid (II), which did not change under conditions favoring enolization. This stable isomer must be a trans-isomer.



To prove the cis-configuration of acid (III), we reduced the carbonyl group in trans-keto acid (II) using the Clemmensen method as modified by Martin [4] for keto acids. This gave trans-2-(p-methoxyphenyl)-cyclopentane--1-acetic acid (V) with m.p. 55-56°, as the asymmetric centers are not involved in the reduction of the keto group.

To prove the syn-cis-configuration of lactone (IV), we reduced the carbonyl group in trans-keto acid (II) with sodium borohydride. The reaction proceeded sterically to form 73.6% anti-trans-hydroxy acid (VI) with m.p. 86-87° and 24% anti-cis-hydroxy acid, isolated as the lactone (VII) with m.p. 141-142°. Hydroxy acid (VI), obtained from trans-keto acid (II), did not lactonize even after prolonged treatment with hydrochloric acid solution. This proves its anti-trans-configuration according to the rule given by Alder and Stein [5]. On the contrary, lactones(VII) and (IV), which are diastereoisomers, could not be opened either by careful acidification of the sodium salt to a neutral reaction (a hydroxy acid could have been formed) or by treatment of the silver salt of the hydroxy acid with methyl iodide (here one might expect the formation of the corresponding methyl ester). Such stability of the lactone ring is due to the absence of strain in cis-biscyclooctane-(0,3,3).

Thus, we can accept that lactone (IV) with m.p. 67-68° has a syn-cis- and lactone (VII) an anti-cis-configuration.

The results of hydrogenating acid (I) agree with the mechanism, proposed by Weidlich [1] and Teilacker and Drossler [6], for the catalytic hydrogenation of α,β-unsaturated ketones, as shown by the following scheme.

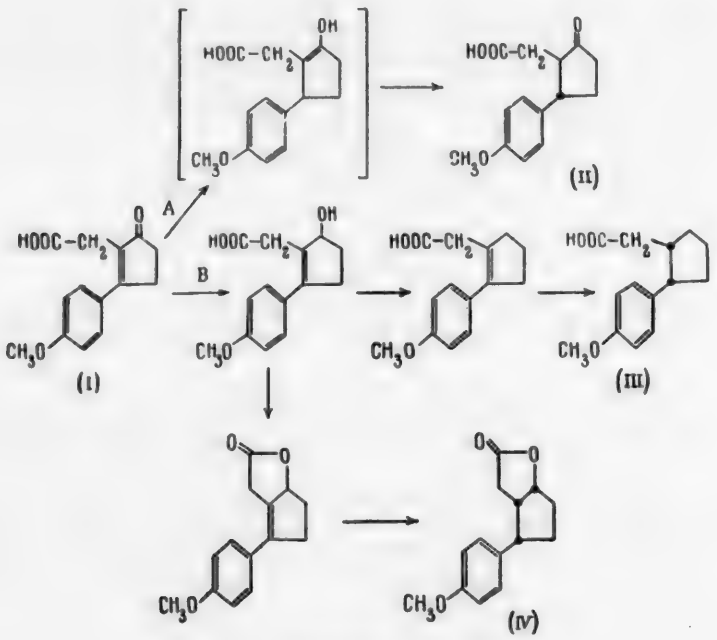
$$R_2C{=}CHCOR \xrightarrow{A} [R_2CHCH{=}C(OH)R] \longrightarrow R_2CHCH_2COR$$
$$\downarrow B$$
$$R_2C{=}CHCH(OH)R \longrightarrow R_2C{=}CHCH_2R \longrightarrow R_2CHCH_2CH_2R$$

Hydrogen may be added either at the C=C (A direction) or C=O (B direction) double bond. In the first case, a saturated ketone is produced which under conditions favoring enolization, is converted into a stable form of ketone (trans- or cis-). A saturated ketone may also be formed as a result of 1,4-addition of hydrogen followed by the conversion of the enol to a stable form of ketone. In the second case, an unsaturated alcohol of an allyl type is formed, which is very readily reduced further under the experimental conditions, to form a saturated hydrocarbon. The authors were unable to isolate the intermediate products. Direction B assumes 1,2-addition of hydrogen, which is analogous to the hydrogenation of an isolated multiple bond [7] and therefore, gives, as a rule, a cis-hydrocarbon.

In our case, when acid (I) was hydrogenated in an alkaline and neutral medium, trans-keto acid (II) was formed by scheme A and cis-acid (III) by scheme B. The syn-cis-hydroxy acid lactone (IV) could have been formed only from an intermediate, unsaturated lactone, whose double bond was activated by the aromatic ring and therefore readily reduced under the experimental conditions. In the case of hydrogenation in an acid medium, the reaction

proceeded only by direction B; therefore the saturated ketone could not be isolated.

Using the reduction of 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid as an example, the mechanism of the reduction of α,β-unsaturated ketones may be represented by the following scheme.



EXPERIMENTAL

Catalytic Hydrogenation of 3-(p-Methoxyphenyl)-Δ^2-cyclopenten-1-one-2--acetic Acid

1. Hydrogenation in neutral medium. 31 g of the acid (I) was hydrogenated in an autoclave in the presence of 10 g of 5% palladium on calcium carbonate as catalyst in 210 ml of methyl alcohol with 3 atmospheres of hydrogen until the absorption of hydrogen ceased (1.3 moles). The catalyst was then filtered off and washed with methanol. The methyl alcohol was distilled off in vacuum to leave a colorless, immobile oil, consisting of three substances, which were separated in two ways.

a) First method. The oil was dissolved in benzene. The acids were extracted from the benzene solution by shaking the latter with 5-6 portions of 5% sodium carbonate solution (50 ml each). Careful acidification of each portion of the soda solution gave a precipitate of acid. The first three fractions contained trans-(p-methoxyphenyl)--cyclopentan-1-one-2-acetic acid as right prisms. The precipitate was filtered off and washed with water on the filter to a neutral reaction to litmus. We obtained 23.9 g of acid (II) with m.p. 104-105°; after recrystallization from 50% alcohol the substance had m.p. 106.5-107.5°. The yield was 77%. The acid (II) was very readily soluble in almost all organic solvents, difficultly soluble in benzine and slightly more soluble in ether.

Found %: C 67.73; H 6.55. $C_{14}H_{16}O_4$. Calculated %: C 67.72; H 6.49.

The fifth and sixth fractions contained 2.5 g of the acid (III) in the form of fine needles with m.p. 73-74°. The yield was 8.5%. The substance was readily soluble in almost all organic solvents, apart from benzine.

Found %: C 71.72; H 7.68. $C_{14}H_{18}O_3$. Calculated %: C 71.77; H 7.74.

The fourth fraction contained 3.2 g of a mixture of the two acids (II) and (III) which had m.p. 65-69°; acid (II) was separated from this mixture by conversion to the semicarbazone.

Evaporation of the original benzene solution yielded 1.7 g (5.8%) of the syn-cis-lactone (IV) in the form of platelets, agglomerated as nodules, with m.p. 66-67°. After recrystallization from a 5-fold amount of an ether – benzene mixture (1 : 4), the substance had m.p. 67-68°. The lactone was readily soluble in alcohol, benzene and chloroform and difficultly soluble in ether and benzine; it dissolved in an aqueous solution of alkali and immediately lactonized on acidification.

Found %: C 72.30; H 6.97. $C_{14}H_{16}O_3$. Calculated %: C 72.39; H 6.94.

b) Second method. The oil was dissolved in 100 ml of ether. After cooling, the solution gradually deposited a precipitate of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid (II), which was filtered off and washed with a small amount of ether on the filter. We obtained 22.1 g of the acid with m.p. 106.5-107.5° (70.9%). The ether mother liquors, which contained a mixture of the trans-keto acid (II), the cis-acid (III) and the syn-cis-lactone (IV) was worked up by the method described above.

The methyl ester of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid was prepared by reacting the silver salt of the acid with methyl iodide and formed colorless prisms with m.p. 39.6-41°, which were readily soluble in all organic solvents, except for benzine.

Found %: C 68.99; H 6.93. $C_{15}H_{18}O_4$. Calculated %: C 68.68; H 6.92.

The semicarbazone of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid formed colorless crystals with m.p. 184° (with decomp.) after recrystallization form alcohol.

Found %: N 13.83. $C_{15}H_{19}O_4N_3$. Calculated %: N 13.76.

To decompose the semicarbazone of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid, a mixture of 3.35 g of the semicarbazone, 2.2 ml of 38% formaldehyde solution and 15 ml of 80% acetic acid was slowly heated to 70°. The semicarbazone dissolved completely. The reaction mixture was kept at 70° for 1 hour. After cooling, the reaction mixture was poured into water. The precipitated acid was extracted with benzene. The benzene extract was washed with water until neutral to litmus and dried with anhydrous sodium sulfate. The benzene was distilled off in vacuum to yield 2.7 g (quantitative yield) of acid (II) with m.p. 102-104°. After recrystallization from 50% alcohol, the substance had m.p. 106.5-107.5°.

2. Hydrogenation in acid medium. a) Hydrogenation with Pd/$BaSO_4$. To 0.5 g of previously reduced 2% palladium on barium sulfate in 20 ml of chemically pure methyl alcohol was added 1 g of acid (I) and 2 ml of 6 N hydrogen chloride in methyl alcohol. The hydrogenation was performed at atmospheric pressure and room temperature. The absorption of hydrogen ceased after the absorption of 3 moles (30 minutes). The catalyst was filtered off and washed with methyl alcohol. After distilling off the solvent we obtained a quantitative yield of acid (III) with m.p. 73-74°, which did not depress the melting point of the acid obtained after hydrogenation in neutral or alkaline solutions.

b) Hydrogenation with Pd on charcoal. 2 g of acid (I) was hydrogenated in the presence of 1 g of 5% palladium chloride on charcoal in 30 ml of methyl alcohol at room temperature and normal pressure. The hydrogen chloride liberated during the reduction of the catalyst provided the acid medium. The absorption of hydrogen stopped after the addition of 3 moles. The isolation was as in the previous experiment. We obtained a quantitative yield of acid (III) with m.p. 73-74°.

c) Hydrogenation up to the addition of 1 mole of hydrogen. 1 g of acid (I) was hydrogenated in the presence of 0.5 g of 2% palladium on barium sulfate in 20 ml of methyl alcohol in an acid medium. The absorption of hydrogen was stopped when 1.05 moles had been absorbed. The catalyst was filtered off. The residue from evaporation of the methyl alcohol was treated with 10 ml of ether. The ether-insoluble precipitate was filtered off to give 0.65 g of the starting acid (I) with m.p. 145-146°. After evaporation of the solvent, the ether solution yielded 0.25 g of acid (III) with m.p. 73-74° (after recrystallization from a mixture of benzine and ether).

Trans-2-(p-methoxyphenyl)-cyclopentane-1-acetic acid (V). The acid (V) was obtained by a Clemmensen reduction of acid (II). To prepare amalgamated zinc, a mixture of 20 g of zinc turnings, 2 g of mercuric chloride, 30 ml of water and 1 ml of concentrated hydrochloric acid was shaken for 5 minutes. The aqueous solution was decanted, the amalgamated zinc treated with 15 ml of water, 30 ml of concentrated hydrochloric acid and 20 ml of toluene and 10 g of acid (II) added. The reaction mixture was boiled vigorously for 30 hours. During this time 10 ml portions of concentrated hydrochloric acid were added every 6 hours. The reaction mixture was cooled, the

toluene layer separated and the aqueous layer extracted with benzene. The toluene–benzene extract was washed with water until neutral to litmus and dried with anhydrous sodium sulfate. Distilling off the solvent left a colorless oil, which quickly crystallized in the form of needles. After recrystallization from petroleum ether, we obtained 7.1 g (75%) of acid (V) with m.p. 54.5-55.5° – the diastereoisomer of the acid (III), obtained after catalytic hydrogenation of acid (II). The substance was readily soluble in almost all organic solvents.

Found %: C 72.05; H 7.63. $C_{14}H_{18}O_3$. Calculated%: C 71.77; H 7.74.

Reduction of trans-3-(p-methoxyphenyl)-cyclopentan-1-one-acetic acid with sodium borohydride. To a solution of the sodium salt, prepared from 12.4 g of acid (II) and 2.18 g of 92% sodium hydroxide in 70 ml of water, was added a solution of 3 g of sodium borohydride in 50 ml of water. The reaction mixture was allowed to stand for 1 hour at room temperature and then the excess sodium borohydride was decomposed with several drops of acetic acid. Then the reaction mixture was made weakly acid to litmus with dilute hydrochloric acid. The precipitate formed was extracted with chloroform. The anti-trans-hydroxy acid (VI) was washed out of the chloroform extract by shaking the latter with 5% soda solution. After acidification of the combined soda solutions, the precipitate formed was filtered off, washed with water and dried. We obtained 9.5 g (76%) of acid (VI) with m.p. 84.5-86°; recrystallization from 20 ml of benzene yielded 9.19 g (73.6%) of acid (VI) with m.p. 86-87°. The substance was readily soluble in alcohol, acetone, ether, benzene and chloroform and difficultly soluble in benzine.

Found %: C 67.22; H 7.26. $C_{14}H_{18}O_4$. Calculated %: C 67.18; H 7.25.

Evaporation of the ether solution yielded 2.8 g (24%) of lactone (VII) with m.p. 141-142° (after recrystallization from alcohol). The lactone anti-cis-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid was the diastereoisomer of lactone (IV) with m.p. 67-68°, obtained after catalytic hydrogenation. The lactone (VII) was difficultly soluble in ether, benzene and benzine and slightly more soluble in chloroform and alcohol.

Found %: C 72.63; H 7.03. $C_{14}H_{16}O_3$. Calculated %: C 72.40; H 6.94.

Anti-trans-3-(p-methoxyphenyl)-cyclopentane-1-acetoxy-2-acetic acid. To 1.25 g of the anti-trans-hydroxy acid (VI), placed in a Claisen flask, was added 1.25 ml of acetyl chloride. The reaction mixture gave off heat. As soon as the precipitate dissolved (1-2 minutes), the excess acetyl chloride was distilled off in vacuum. The oily residue crystallized after standing for several hours. Two recrystallizations from a mixture of benzene and benzine yielded 1.05 g of anti-trans-3-(p-methoxyphenyl)-cyclopentane-1-acetoxy-2-acetic acid with m.p. 91.5-92°. The yield was 72%. The substance was readily soluble in the usual organic solvents with the exception of benzine.

Found %: C 65.99; H 6.91. $C_{16}H_{20}O_5$. Calculated %: C 65.73; H 6.90.

Attempted preparation of the methyl ester of syn-cis-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid. 1.67 g of the syn-cis-lactone of the hydroxy acid (IV) was boiled with a solution of 0.49 g of 87% potassium hydroxide in 30 ml of water for 0.5 hours. During this time the lactone dissolved completely. The solution was cooled and to it was added 30 ml of methyl alcohol and a solution of 1.24 g of silver nitrate in 8.5 ml of water. A white precipitate of the silver salt formed immediately. After 10 minutes mixing, 9.4 g of methyl iodide was added. After a further 15 minutes mixing, the yellow precipitate of silver iodide formed was filtered off. The mother liquor was evaporated down to yield an oily substance, which was extracted with ether. The ether extract was washed with water and dried with anhydrous sodium sulfate. Evaporation of the solvent yielded 1.6 g of syn-cis-lactone (IV) with m.p. 66-68°, which did not depress the melting point of the original lactone.

Attempted preparation of the methyl ester of anti-cis-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid. Under the reaction conditions described above, the trans-lactone of 3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid (VII) also gave a quantitative yield of the starting lactone with m.p. 141-142°.

SUMMARY

1. The catalytic hydrogenation of 3-(p-methoxyphenyl)-Δ^2-cyclopenten-1-one-2-acetic acid in the presence of a palladium catalyst was studied in an acid and in alkaline and neutral media. It was established that hydrogenation in an alkaline and in a neutral medium gave 3 substances: trans-3-(p-methoxyphenyl)-cyclopentan-1-one-2-acetic acid, the lactone of syn-cis-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid and cis-2-(p-methoxyphenyl)-cyclopentane-1-acetic acid, while hydrogenation in an acid medium gave the latter exclusively.

2. It was shown that reduction of the carbonyl group of trans-3-(p-methoxyphenyl)-cyclopentan-2-one-2--acetic acid with sodium borohydride proceeded sterically to form 73% of anti-trans-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid; the other epimer was isolated in the form of the lactone of anti-cis-3-(p-methoxyphenyl)-cyclopentan-1-ol-2-acetic acid (24%).

3. The isolation of the intermediate alcohol (the hydroxy acid in the form of its lactone) confirmed the mechanism proposed earlier for the catalytic hydrogenation of α,β-unsaturated ketones.

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RESIN ACIDS

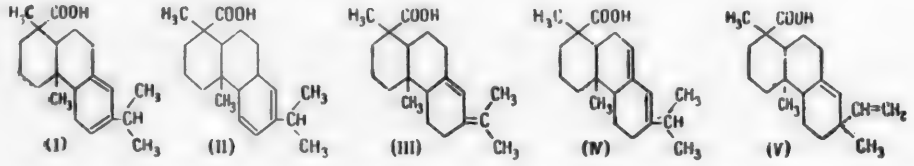
I. THE NATURE OF α-SAPINIC ACID

I. I. Bardyshev and V. V. Kokhomskaia

α-Sapinic acid was first isolated by Dupont and Dubourg [1] from the soft resin of Pinus maritima Mill. It was later also isolated from the soft resin of native, coniferous Pinus silvestris L. [2, 3] and Picea excelsa Link[4]. According to these investigations, α-sapinic acid constitutes about 55% of the total of resin acids from soft resin, which are a large-scale product of the wood pulp chemical industry of the USSR. V. N. Krestinskii et al.[5] and V. M. Akulovich [6] devoted their investigations to determining the structural formula of α-sapinic acid. D. V. Tishchenko et al. [7] studied the autooxidation of α-sapinic acid and the structure of the higher autooxidation product of this acid. As can be seen from these papers, the majority of the Soviet investigators consider α-sapinic acid to be an individual resin acid. B. A. Arbuzov [8] was the only one who had some doubt on the individuality of α-sapinic acid.

In studying the composition of resin acids in soft resins of various native conifers [9, 10], we could not ignore the problem of the individuality of α-sapinic acid.

The present investigation showed that the so-called α-sapinic acid is not a single acid but is a complex mixture consisting of levopimaric (I), palustric (II), neoabietic (III), abietic (IV) and dextropimaric (V) resin acids. It should be noted that the structure of palustric acid (II) has not yet been established definitely [11].



EXPERIMENTAL

α-Sapinic acid was isolated from the resin of Pinus silvestris by the method of Krestinskii et al. [2] and had m.p. 146-148° and $[\alpha]_D$ −64.6°. Its ultraviolet absorption spectrum is shown in Fig. 1 (Curve 1). According to its properties, the α-sapinic acid we isolated was identical to the α-sapinic acid obtained by Krestinskii et al.

Isolation of levopimaric acid. To a solution of 150 g of α-sapinic acid in 350 ml of ether was added 100 g of a saturated ether solution of bornylamine in small portions. The reaction mixture was left for 12 hours at room temperature then the salt formed was filtered off and washed many times on the filter with ether. We obtained 151 g of the bornylamine salt (salt A) with m.p. 135-149° and $[\alpha]_D$ −59.6°. The UV-spectrum of salt A is shown in Fig. 1 (Curve 2). The first crystallization of the salt from alcohol gave 50 g of a crystalline product with m.p. 165-175° and $[\alpha]_D$ −165.0°, and after three recrystallizations we obtained 5 g of the salt of bornylamine and levopimaric acid with m.p. 185-187° and $[\alpha]_D$ −191.2°. Its UV-spectrum is shown in Fig. 1 (Curve 3). To isolate free levopimaric acid, 2 g of the salt obtained was decomposed with an aqueous solution of boric acid and the mixture extracted with ether. The ether layer was separated, washed with water and dried with magnesium sulfate. The residue from evaporation of the ether was recrystallized three times from alcohol to yield 0.06 g of levopimaric acid (Table and Fig. 1, Curve 4).

Isolation of palustric acid. The ether mother liquor, obtained after separation of the bornylamine salt A, was treated with an aqueous solution of boric acid. The acid remaining after evaporation of the ether was dissolved in acetone and 13.5 g of diethylamine was added to the solution. The salt obtained was recrystallized from acetone. Five recrystallizations yielded 1.7 g of the salt of diethylamine and palustric acid with m.p. 133.5-138.5° and $[\alpha]_D$ + 50.7°. Its UV-spectrum is shown in Fig. 2 (Curve 2). Further recrystallization of the salt did not change its specific rotation or specific absorption coefficient. As a result of decomposing this salt (1.55 g) with boric acid and recrystallizing the products obtained 3 times from alcohol, we isolated 0.12 g of palustric acid (Table and Fig. 2, Curve 3). Elementary analysis of the acid confirmed the formula $C_{20}H_{30}O_2$.

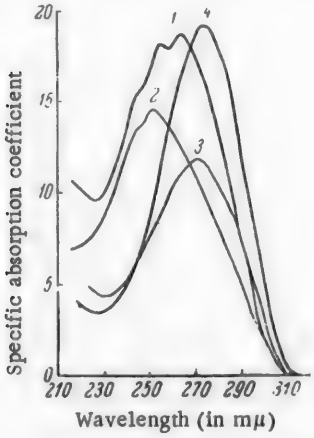


Fig. 1. Ultraviolet absorption spectra. 1) α-sapinic acid; 2) bornylamine salt A; 3) salt of bornylamine and levopimaric acid; 4) levopimaric acid.

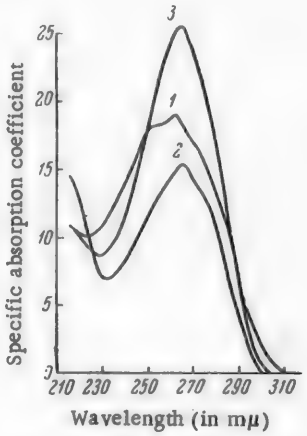


Fig. 2. Ultraviolet absorption spectra. 1) α-sapinic acid; 2) salt of diethylamine and palustric acid; 3) palustric acid.

Isolation of neoabietic acid. The mother solution, remaining after the isolation of the diethylamine salt of palustric acid, was treated with boric acid to regenerate resin acids. The acids obtained were converted to the bornylamine salts and recrystallization of these from ether gave a bornylamine salt with m.p. 120-138° and $[\alpha]_D$ −15.3°. The latter was combined with the bornylamine salt obtained from the mother solution left after separation of levopimaric acid. The resin acids (47 g), obtained by decomposing the salt fractions described above with boric acid had $[\alpha]_D$ −15.0°. To remove levopimaric acid under conditions excluding isomerization, 50 ml of petroleum ether distilled over sodium was added to the mixture of acids obtained, followed by 10 g of twice-distilled maleic anhydride in 10 ml of dry acetone. At this the temperature rose from 23 to 32°. The reaction mixture was left at room temperature for 12 hours and then it was poured into 433 ml of 3% sodium hydroxide solution. The petroleum ether was separated and the solution diluted to 2.6 liters with water and acidified to pH ≈ 6 with dry boric acid. The acids which had not reacted with maleic anhydride were precipitated with sodium sulfate, filtered off, washed several times with distilled water on the filter and dissolved in ether. The ether layer was separated and dried with magnesium sulfate. The mixture of resin acids obtained had $[\alpha]_D$ + 52.3°. To the ether solution of this mixture of acids was added 6.5 g of ethanolamine. The product formed was filtered off and washed with ether on the filter. We obtained 27 g of an ethanolamine salt with m.p. 113-134° and $[\alpha]_D$ + 49.7° and recrystallization of this from ethyl acetate gave 13 g of an ethanolamine salt with $[\alpha]_D$ + 61.5°. The latter was decomposed with an aqueous solution of boric acid. The residue from evaporation of the ether was dissolved in acetone and 3.5 ml of diethylamine was added to the acetone solution. The salt formed was filtered off and washed with acetone on the filter. We obtained 10 g of a diethylamine salt (salt B) with m.p. 107-116.5° and $[\alpha]_D$ + 67.1° (The UV-spectrum is shown in Fig. 3, Curve 2). Two recrystallizations of this product from acetone yielded the salt of neoabietic acid and diethylamine with m.p. 152-155° and $[\alpha]_D$ + 120.6°. (The UV-spectrum is shown in Fig. 3, Curve 3). 0.55 g of the neoabietic acid salt was decomposed with an aqueous solution of boric acid. The residue from evaporation of the ether was recrystallized twice from alcohol; we thus isolated 0.07 g of neoabietic acid (Table and Fig. 3, Curve 4).

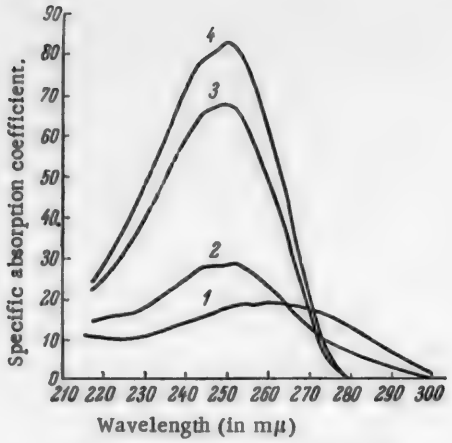


Fig. 3. Ultraviolet absorption spectra. 1) α-Sapinic acid; 2) diethylamine salt B; 3) salt of diethylamine and neoabietic acid; 4) neoabietic acid.

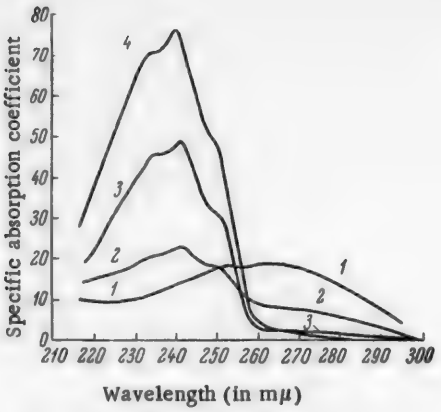


Fig. 4. Ultraviolet absorption spectra. 1) α-Sapinic acid; 2) bornylamine salt C; 3) salt of bornylamine and abietic acid; 4) abietic acid.

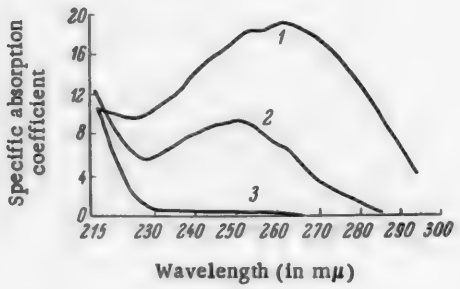


Fig. 5. Ultraviolet absorption spectra. 1) α-Sapinic acid; 2) ethanolamine salt D; 3) salt of ethanolamine and dextropimaric acid.

Isolation of abietic acid. The resin acids were regenerated with boric acid by the usual method from the mother liquors obtained after the isolation of the ethanolamine salt of neoabietic acid with $[\alpha]_D$ + 49.7 and +61.5°. To an alcohol solution of the acids was added 10 g of a saturated ether solution of bornylamine. The product formed was filtered off and washed with alcohol on the filter. We obtained 4.7 g of a bornylamine salt (salt C) with m.p. 131.5-137.5° and $[\alpha]_D$ +16.6°. (The UV-spectrum is shown in Fig. 4, curve 2). Four recrystallizations of this fraction from alcohol yielded 0.25 g of the salt of bornylamine and abietic acid with m.p. 155-156.5° and $[\alpha]_D$ −47.5° (The UV-spectrum is shown in Fig. 4, Curve 3). 0.2 g of the abietic acid salt was decomposed with boric acid. The residue from evaporation of the ether was recrystallized from alcohol; this yielded 0.045 g of abietic acid (Table and Fig. 4, Curve 4).

Physical Properties of Resin Acids Isolated from α-Sapinic Acid (Upper Series of Figures) and Comparison of them with Literature Data

Name of acid	Melting point	$[\alpha]_D$ of alcohol solution	Specific absorption coefficient	Position of absorption maximum (in mμ)
Levopimaric acid	150—152°	—277.0°	19.3	272.5
According to literature data [12,13]	150—152	—275.0	19.2	272.0
Neoabietic acid	169—170.5	+162.7	81.4	250—251
According to literature data [10]	177.5—179	+175.0	80.5	250—251
Abietic acid	170—172	—105.6	75.6	241
According to literature data [9]	174—175	—116.0	85.0	241
Palustric acid	167.5—169.5	+ 71.4	25.5	266
According to literature data [11]	162—167	+ 71.8	31.0	265—266

Isolation of ethanolamine salt of dextropimaric acid. From the mother solution, obtained after the isolation of the bornylamine salt with m.p. 120-138° and $[\alpha]_D$ −15.3° (see section on neoabietic acid), we regenerated the resin acids and then converted the latter into the ethanolamine salt. Recrystallization of this salt from ethyl acetate gave a second fraction of crystals (0.2 g) with m.p. 146.5-154.5° (salt D; Fig. 5, Curve 2). After 3 recrystallizations of this fraction from ethyl acetate, we isolated 0.02 g of the ethanolamine salt of dextropimaric acid with m.p. 164-166° and $[\alpha]_D$ +49.5° (The UV-spectrum is shown in Fig. 5, Curve 3). The ethanolamine salt, prepared from a sample of dextropimaric acid with m.p. 218-219°, melted at 167-169°.

SUMMARY

1. The so-called α-sapinic acid, isolated from the soft resin of Pinus silvestris by the method of Krestinskii et al., is not an individual acid, but is a mixture of levopimaric, palustric, neoabietic, abietic and dextropimaric resin acids.

2. Palustric acid was isolated from the soft resins of Pinus silvestris for the first time.

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*Original Russian pagination. See C. B. Translation.

RESIN ACIDS

II. THE NATURE OF β-SAPINIC ACID

I. I. Bardyshev and L. I. Ukhova

β-Sapinic acid was first isolated from the soft resin of Pinus maritima Mill. According to Dupont [1], this soft resin consists of the following acids: α-sapinic (49%), β-sapinic (21%), levopimaric (21%) and dextropimaric (9%). Krestinskii et al. [2] found that the soft resin of Pinus silvestris L. contained β-sapinic acid (5%), in addition to α-sapinic (55%), levopimaric (30%) and dextropimaric (10%) acids.

However, the structural formula of β-sapinic acid was not established. Furthermore, the problem of whether this acid is an individual acid has not yet been solved [3].

The present investigation showed that β-sapinic acid, obtained by the method of Krestinskii, is not an individual acid, but consists of levopimaric (about 60%), neoabietic and abietic acids. It is also possible that other resin acids are included in small amounts in the composition of β-sapinic acid.

EXPERIMENTAL

β-Sapinic acid. We isolated this acid from the soft resin of Pinus silvestris by the method of V. N. Krestinskii [2] and it had m.p. 139-143° and $[\alpha]_D$ −94.5°. Its UV-spectrum is shown in Fig. 1, Curve 1. In all, 40 kg of soft resin was processed; from it we obtained 24 kg of mixed resin acids, from which we isolated 200 g of β-sapinic acid.

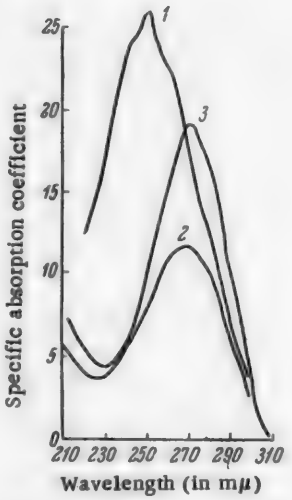

Fig. 1. Ultraviolet absorption spectra. 1) β-Sapinic acid; 2) bornylamine salt of levopimaric acid; 3) levopimaric acid.

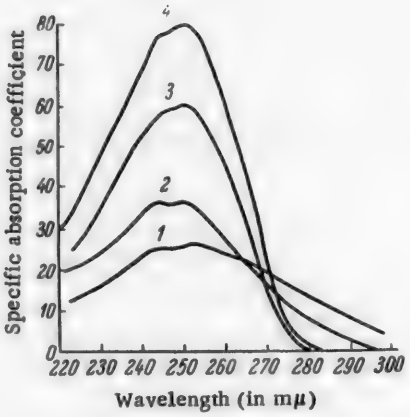

Fig. 2. Ultraviolet absorption spectra. 1) β-Sapinic acid; 2) resin acids, which do not react with maleic anhydride; 3) diethylamine salt of neoabietic acid; 4) neoabietic acid.

Isolation of levopimaric acid. To 180 g of a solution of β-sapinic acid in ether was added 90 g of bornylamine as an ether solution. The product was washed with ether and dried to yield 248 g of the bornylamine salt of β-sapinic acid with m.p. 128-152° and $[\alpha]_D$ −79.1°. 40 g of the salt was recrystallized 3 times from alcohol; as a result we obtained a salt with m.p. 185-187° and $[\alpha]_D$ −179° (its UV-spectrum is shown in Fig. 1, Curve 2). The salt was decomposed with an aqueous solution of boric acid and the levopimaric acid obtained as a result of this was recrystallized twice from alcohol, when it had the constants: m.p. 149.5-151°, $[\alpha]_D$ −276°, specific absorption coefficient 19.0 at 272 mμ (Fig. 1, Curve 3). Elementary analysis of the acid confirmed the formula $C_{20}H_{30}O_2$.

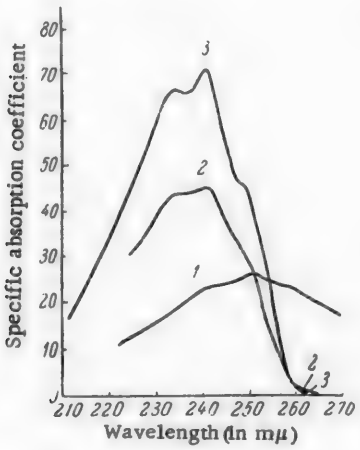

Fig. 3. Ultraviolet absorption spectra. 1) β-Sapinic acid; 2) bornylamine salt of abietic acid; 3) abietic acid.

Isolation of neoabietic acid. β-Sapinic acid (140 g) was treated with maleic anhydride under conditions excluding isomerization [4]. As a result of the treatment we obtained 42.4 g of resin acids which did not react with maleic anhydride and had $[\alpha]_D$ +59° (the UV-spectrum is shown in Fig. 2, Curve 2). To 40 g of an acetone solution of these resin acids was added 10 g of diethylamine dissolved in acetone. The salt formed was washed with acetone and dried. We obtained 33.5 g of crystals with $[\alpha]_D$ +56°, which were recrystallized 4 times from acetone. During this the specific rotation of the salt first increased and then remained constant ($[\alpha]_D$ + 98.7°, +111.5°, +109.8°, + 109.8°). 3.35 g of the diethylamine salt (m.p. 153--157° and $[\alpha]_D$ +109.8°) was decomposed with an aqueous solution of boric acid by the usual method. After two recrystallizations from alcohol, the neoabietic acid obtained in this way had m.p. 179-180.6°, $[\alpha]_D$ +171.2° and a specific absorption coefficient of 79.3 at 250 mμ (Fig. 2, Curve 4). Elementary analysis of the acid confirmed the formula $C_{20}H_{30}O_2$.

Data on x-ray analysis, carried out in the Laboratory of the Physical Chemistry Institute of the Academy of Sciences of the Byelorussian SSR, showed that neoabietic acid has a primitive elementary cell of the rhombic syngony with the axes: a 6.11 A, b13.15 and c 21.39 A.

Isolation of abietic acid. The mother liquors of the diethylamine salts, obtained after the isolation of neoabietic acid, were combined and evaporated to dryness and the salt decomposed with boric acid. To the resin acids was added bornylamine and as a result we obtained 28 g of a salt. After recrystallizing it from alcohol, we isolated 5 g of crystals with m.p. 138-144°. Four recrystallizations from alcohol yielded bornylamine abietate with m.p. 158.5-160.5° and $[\alpha]_D$ −38.6° (the UV-spectrum is shown in Fig. 3, Curve 2). 0.24 g of bornylamine abietate was decomposed with boric acid in the usual way. After two recrystallizations from alcohol, the abietic acid had m.p. 171.5-173°, $[\alpha]_D$ −93°, specific absorption coefficient 70.7 at 241 mμ (Fig. 3, Curve 3). Elementary analysis of the acid confirmed the formula $C_{20}H_{30}O_2$.

SUMMARY

β-Sapinic acid, isolated from the soft resin of Pinus silvestris L. by Krestinskii's method, is not an individual resin acid but is a mixture of levopimaric, abietic and neoabietic acids and, possibly, of small amounts of other resin acids.

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*Original Russian pagination. See C. B. Translation.

INVESTIGATIONS IN THE FIELD OF QUINOLINE DERIVATIVES

XVII. SYNTHESIS OF SOME 6- AND 8-ALKOXYQUINOLINES

B. I. Ardashev and V. I. Minkin

The ethers of 6- and 8-hydroxyquinolines are used for preparing cyanine dyes and medicines. The absence of an effective method for controlling the vigorous course of the Skraup reaction [1] and the low yields of 8-alkoxyquinolines, due to steric hindrance, are some of the disadvantages of the existing methods for synthesizing these ethers.

For various reasons [2] the method of adding a double amount of H_2SO_4 to the reaction mixture [3], the use of Kone's modification [4] and the direct introduction of acrolein into the reaction [5] cannot be recommended. We did not obtain satisfactory results in trying to obtain alkoxyquinolines directly from nitro compounds (in analogy with Das' work) or by using dilute H_2SO_4, used previously in some works [6-9].

A good yield with a smooth reaction course was achieved by gradually adding (over a period of 10-20 minutes) a mixture of amine, sulfuric acid and glycerin to the oxidizing agent, heated to a temperature above that of the reaction. Walter [10] was the first to propose this method; Manske [11] recently recommended it. Our modification is preferable to the alkylation of 8-hydroxyquinoline [12, 13] or the synthesis using arsenic acid by Knueppel's method [14, 15].

EXPERIMENTAL

The syntheses were performed in a three-necked flask, fitted with a mechanical stirrer, a reflux condenser and a thermometer.

6-Methoxyquinoline. 11 g of p-nitroanisole was heated to 170° and over a period of 30-60 minutes a mixture of 13 g of p-anisidine, 12.5 ml of sulfuric acid (s.g. 1.82) and 60 g of glycerin, kept at the temperature of a water bath, was introduced through the condenser. Toward the end of the addition, the temperature of the gently boiling mixture was 150° and after a further 5-5.5 hours, 134°. The remainder of the p-nitroanisole was removed by steam distillation, the mixture made alkaline and then the 6-methoxyquinoline distilled off in steam (p-anisidine does not distill over at this point [16]). We isolated 10.8 g (64%) of 6-methoxyquinoline. The b.p. was 127-130° (at 5 mm). The picrate had m.p. 209°; the iodomethylate had m.p. 236°.

8-Methoxyquinoline. We used 10 g of o-anisidine, 29 g of glycerin, 12 ml of sulfuric acid and 12 g of o-nitroanisole. The mixture was heated for 3.5 hours. The temperature at the beginning of the reaction was 200° and at the end, 133°. We obtained 4.9 g (38%) of 8-methoxyquinoline with b.p. 155° (13 mm). The picrate had m.p. 162.5°; the iodomethylate had m.p. 161°.

8-Ethoxyquinoline. To 7 g of o-nitrophenol and 1 g of $FeSO_4 \cdot 7H_2O$, at 150° was added a heated mixture of 13.7 g of o-phenetedine, 18 ml of sulfuric acid (s.g. 1.82) and 30g of glycerin. At the end of the addition (after approximately 18 minutes) the temperature was 150° and after a further 2 hours, 137°. The whole of the o-nitrophenol reacted and none distilled off with steam. The mixture was made alkaline and extracted twice with large amounts of benzene for better separation of the layers. The tar was filtered off from the benzene extract, which was washed, the benzene distilled off, the residue dissolved in ether and the ether extract filtered free from tar and treated twice with phthalic anhydride (portions of 10 and 6 g) to separate the tertiary amine [17]. The phthalaminic acid formed was extracted with 10% sodium hydroxide solution. Evaporation of the ether yielded 6.8 g

(39.7%) of 8-ethoxyquinoline. The b.p. was 200° (29 mm). The picrate had m.p. 180°; the iodomethylate had m.p. 199°.

6-Ethoxyquinoline. 10 g of p-phenetedine, 39 g of glycerin, 9 ml of sulfuric acid and 7.5 g of o-nitrophenol were used. The mixture was heated for 5.5 hours. The temperature at the beginning of the reaction was 160° and at the end, 137°. We obtained 6.3 g (50%) of 6-ethoxyquinoline with b.p. 289°. The picrate had m.p. 194°; the iodomethylate had m.p. 196°.

SUMMARY

A method for synthesizing the ethers of 6- and 8-hydroxyquinolines was developed from Walter's modification, with greater yields than those obtained by known methods.

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INVESTIGATION OF THE CRYSTALLINE SUBSTANCE FORMED IN THE PRODUCTION OF ANABASINE SULFATE

A. S. Labenskii

In the technical process of producing anabasine sulfate from Anabasis aphylla there is a stage in which the kerosene solution of the total alkaloids is treated with dilute sulfuric acid to obtain the commercial product. It was noted repeatedly that at this stage a crystalline deposit of unknown composition was precipitated from the sulfuric acid solution of the total alkaloids. Investigation of this deposit was of considerable interest and became the aim of this work.

The deposit, obtained from the Chimkent chemical pharmaceutical plant, was purified by recrystallization from dilute isopropyl alcohol. The crystals dissolved readily in water but were insoluble in most of the usual organic solvents. An aqueous solution had an acid reaction (pH 2.8), contained a large amount of SO_4'' ions, gave a voluminous precipitate when tested with silicotungstic acid and had optical activity.

One could surmise that the deposit was the sulfate of some organic base. Attempts to isolate the organic base (which we denoted temporarily as "substance A") from an aqueous solution of this salt by making alkaline and then extracting with organic solvents (ether, benzene, chloroform) did not give positive results as substance A did not pass into the organic solvent. From this fact we assumed that substance A was an amino acid. We isolated it. An elementary analysis of substance A showed that its composition was similar to that of aphyllinic acid [1]. Some of the properties of these substances were also similar. A mixed melting point of substance A with aphyllinic acid showed no depression (the aphyllinic acid was obtained from aphylline hydrochloride [2] by hydrolyzing the aphylline with dilute sulfuric acid). There was also no depression in the melting point of a mixture of the methyl esters, prepared by the method of Orekhov [3] and Späth et al. [1] from aphyllinic acid and substance A.

One can conclude from these facts that substance A is aphyllinic acid. It follows from this that the crystalline material, separated during the process of anabasine sulfate production was mainly the sulfate of this amino acid.

The presence of aphyllinic acid in technical anabasine sulfate may be explained only by its formation from aphylline on treatment with sulfuric acid during the process. Späth [1] had indicated such a possibility in his paper. This is all the more probable as during the extraction of the alkaloids from the kerosene solution, the reaction mass heats up and this would promote aphylline hydrolysis.

The precipitation of aphyllinic acid sulfate from an aqueous solution of the alkaloid anabasine sulfate mass, in spite of its high solubility in water, may be explained by salting out.

Assuming that during the production process, simultaneously with the hydrolysis of aphylline, the hydrolysis of aphyllidine should occur, we decided to search for aphyllidinic acid in technical anabasine sulfate. As aphyllidinic acid is not described in the literature (directions are given only for preparing its ethyl ester [3]) we first prepared aphyllidinic acid, starting from the aphyllidine we had available, by hydrolyzing the latter with dilute sulfuric acid. We obtained the aphyllidinic acid in the form of crystals and characterized it by melting point and specific rotation.

By suitably working over technical anabasine sulfate, we also isolated aphyllidinic acid from the latter. Direct comparison showed that this acid was identical to the aphyllidinic acid, obtained by hydrolyzing aphyllidine.

In studying the properties of aphyllinic acid, we established that when heated to melting it decomposed to form aphylline (about 80% yield). This has made it possible to prepare aphylline quite readily from the waste

products of anabasine sulfate production, of which aphyllinic acid sulfate is one. It is possible that such a method for producing aphylline may be of practical value, as according to data in the literature [4], aphylline is a pharmacologically active substance (anesthesia).

In investigating the substance obtained during the melting of aphyllinic acid hydrochloride, we isolated a small amount of a crystalline, optically active substance that was isomeric with aphylline. We obtained the same substance from the reaction mass, obtained by heating aphylline hydrochloride to 265°. We may surmise that this substance, which we temporarily denoted as "substance B", may be one of the eight possible stereoisomers of sparteine with an oxo group in the inner ring, the more so as some of the properties of this substance are quite similar to those of oxo-β-isosparteine [5]. The study of this substance is being continued.

EXPERIMENTAL

a) Purification of starting material. 100 g of the commercially obtained deposit was recrystallized 3 times from 65% isopropyl alcohol. We obtained 71.5 g of lustrous, white plates. After drying in vacuum over P_2O_5 (85°, 2-4 mm), the substance had m.p. 214-215°; $[\alpha]^{20}D$ +7.25° (water, c 10.6).

Found %: C 49.2; H 7.62; N 7.55; S 8.42; SO''_4 26.25. $C_{15}H_{26}O_2N_2 \cdot H_2SO_4$. Calculated %: C 49.42; H 7.74; N 7.68; S 8.78; SO''_4 26.35.

b) Isolation of substance A. 10 g of the sulfate of substance A was dissolved in 100 ml of water with gentle heating. Powdered $Ba(OH)_2$ was added until there was an alkaline reaction to phenolphthalein. A stream of CO_2 was passed through the mixture until the alkaline reaction disappeared and then the mixture was filtered. The slightly turbid filtrate was purified with active charcoal. The colorless, clear solution was evaporated in vacuum. The dry residue was dissolved in 45 ml of methanol with heating. The solution was treated with activated charcoal. To the clear solution was added an equal volume of anhydrous acetone. A crystalline precipitate in the form of prisms began to form immediately. The weight was 6 g. After drying in vacuum (P_2O_5, 100°, 2-4 mm), the substance had m.p. 217-218°; $[\alpha]^{20}D$ + 14.2° (water, c 5.2).

Found %: C 67.80; H 9.77; N 10.39. $C_{15}H_{26}O_2N_2$. Calculated %: C 67.62; H 9.89; N 10.5.

Substance A was insoluble in chloroform, ether, acetone and dioxan difficultly soluble in anhydrous alcohol, more soluble in 95% alcohol, still more soluble in methanol and readily soluble in water.

By mixing alcohol solutions, we obtained a picrate with m.p. 175-176°.

Found %: N 14.17%. $C_{15}H_{26}O_2N_2 \cdot C_6H_3O_7N_3$. Calculated %: N 14.15.

On acidification of a solution of substance A in methanol with an alcohol solution of HCl (to congo) followed by the addition of acetone, a crystalline precipitate of the dihydrochloride was formed and this had m.p. 252-253° (decomp.), $[\alpha]^{20}D$ +6.4° (water, c 4.4).

Found %: C 52.83; H 8.69; N 7.34; Cl 18.66. (for air-dried material). $C_{15}H_{26}O_2N_2 \cdot 2HCl \cdot C_2H_5OH$. Calculated %: C 52.95; H 8.87; N 7.27; Cl 18.41.

2 g of substance A was dissolved in 30 ml of a 50% solution of HCl in methanol. The solvent was distilled off the following day and the hydrochloride recrystallized from 10 ml of methanol. We obtained 1.5 g of a salt, which was dissolved in water, made alkaline and extracted with ether to give the free base (an oil). Solution of the latter in ethyl acetate gave 0.7 g of the crystalline methyl ester of substance A with m.p. 81-82°. The addition of a methanol solution of HCl to a methanol solution of the substance obtained precipitated crystals of a hydrochloride with m.p. 233-235°.

c) Preparation of aphyllinic acid. A solution of 5 g of aphylline hydrochloride in 15 ml of water was made alkaline with 50% KOH and shaken with benzene (4 × 25 ml). Aphylline was extracted from the benzene solution with 7% H_2SO_4 (2 × 25 ml). The sulfuric acid solution was heated for 5 hours on a water bath. Then the solution was treated with barium hydroxide. The remaining aphylline was extracted from the filtered solution with benzene, then a stream of CO_2 was passed through the alkaline solution. The solution was then treated as described in experiment "b". We obtained 1.5 g of a crystalline precipitate of aphyllinic acid. After recrystallization from methanol, the acid had m.p. 217-218°. It did not depress the melting point of substance A.

1.5 g of aphyllinic acid was treated similarly to substance A in the preparation of its methyl ester (see experi-

ment "b"). We obtained 0.3 g of methyl aphyllinate with m.p. 82-83°. The ester did not depress the melting point of the methyl ester of substance A.

By mixing alcohol solutions of methyl aphyllinate and picric acid we obtained a monopicrate as long yellow needles with m.p. 221-222° (decomp.).

Found %: N 13.49. $C_{16}H_{28}O_2 \cdot C_6H_3O_7N_3$. Calculated %: N 13.79.

d) Preparation of aphyllidinic acid. A solution of 1.9 g of aphyllidine with m.p. 111-112° in 20 ml of 7.5% H_2SO_4 was heated on a water bath for 5 hours. The product was isolated as described in experiment "b". The amino acid was purified by reprecipitation with acetone from a methanol solution. We obtained 1.1 g of aphyllidinic acid in the form of octahedrons. After drying in vacuum (P_2O_5, 60°, 2-4 mm), the substance had m.p. 215--216° (decomp.); $[\alpha]^{20}D$ −8.0° (methanol, c 7). In a test for unsaturation with $KMnO_4$ and H_2SO_4, the reagent was immediately decolorized.

Found %: C 68.0; H 9.21; N 10.4. $C_{15}H_{24}O_2N_2$. Calculated %: C 68.13; H 9.15; N 10.59.

Mixing alcohol solutions of aphyllidinic and picric acids gave an amorphous yellow precipitate. Recrystallization from dilute alcohol with slow cooling, gave short, broad crystals with m.p. 196° (decomp.).

Found %: N 15.40. $C_{15}H_{24}O_2N_2 \cdot 2C_6H_3O_7H_3$. Calculated %: N 15.5.

e) Isolation of aphyllinic and aphyllidinic acids from technical anabasine sulfate. To 250 g of technical anabasine sulfate (which was obtained from the process when significant amounts of aphylline acid sulfate were produced) was added 50% sulfuric acid until there was a strongly acid reaction to methyl orange. The mixture was left for 2 days and then filtered. The residue on the filter was washed with isopropyl alcohol and recrystallized twice from a 65% aqueous solution of the latter. We obtained 25 g of white plates, identical with aphyllinic acid sulfate. To the filtrate (without the wash alcohol) was added water up to 700 ml and then $Ba(OH)_2$ to a strongly alkaline reaction to phenolphthalein. The precipitate of $BaSO_4$ was filtered off. The filtrate was evaporated down to 250 g in vacuum. The alkaloids were almost completely extracted with chloroform. A stream of CO_2 was passed through the alkaline aqueous solution until there was a neutral reaction to phenolphthalein. The precipitate was separated off and the filtrate evaporated to dryness in vacuum. The brown amorphous residue (17 g) was dissolved in 50 ml of methanol and the solution purified with activated charcoal. The filtrate was concentrated to to 35 ml and an equal volume of anhydrous acetone was added to it. The crystalline precipitate formed (2.75 g) was dissolved in 5 ml of CH_3OH with heating. To the solution was again added an equal volume of acetone. Crystals (octahedrons) of aphyllidinic acid with m.p. 215-216° were gradually deposited.

f) Preparation of aphylline from aphyllinic acid. 15 g of aphyllinic acid in a pyrex flask was heated on a bath at 225-235° for 25 minutes. Cooling gave a thick, brownish oil, which was completely dissolved in benzene. The solution was passed through a column containing 100 g of Al_2O_3. The column was eluted with benzene. In all the fractions was a thick, light oil (12.5 g in all). Solution in anhydrous alcohol and the addition of alcoholic HCl yielded crystals of a hydrochloride with m.p. 210-213° (decomp.); $[\alpha]^{20}D$ +11.3° (water, c 3.7). 5.5 g of the hydrochloride obtained was dissolved in water, made alkaline, extracted with petroleum ether, dried with potassium carbonate and distilled to give 4.3 g of a basic oil, which distilled at 185-190° (2-3 mm), $[\alpha]^{20}D$ +13.1° (methanol, c 15.6). By mixing alcohol solutions of this base and picric acid, we obtained crystals with m.p. 230-231° (decomp., from methanol). A mixed melting point with the obtained hydrochloride and the hydrochloride of aphylline and also with the obtained picrolonate and the picrolonate of aphylline was not depressed.

g) Preparation of aphyllidine from aphyllidinic acid. 1.5 g of aphyllidinic acid in a Claisen flask was heated at 220-230° for 20 minutes in a stream of nitrogen. The molten mass was distilled (bath temperature 150°, pressure 2-4 mm). An oil (0.5 g) was distilled and this was dissolved in petroleum ether, chromatographed on Al_2O_3 and eluted with petroleum ether to give crystals (0.25 g) with m.p. 107-108°. After purification via the perchlorate, the substance had m.p. 110-112°. It did not depress the melting point of aphyllidine.

h) Preparation of a new base, isomeric with aphylline. 12.5 g of aphyllinic acid hydrochloride was heated at 265-270° for 25 minutes. The mass melted and gaseous products were evolved. Cooling yielded a light brown glassy mass, which was dissolved in water (the solution gave an acid reaction). The solution was washed with chloroform, made alkaline and extracted with ether. Evaporation of the ether gave a thick brown oil (6.5 g). The oil was dissolved in benzene, chromatographed on Al_2O_3 and eluted with benzene. From the first fractions we obtained 3.1 g of a semicrystalline residue. The residue was sublimed in vacuum (100°, 2-4 mm). We obtained 2.5 g

of white, but slightly oily crystals, which were recrystallized twice from hexane. The m.p. was 105-106°, $[\alpha]^{20}D$ +25.9° (anhydrous alcohol, c 14).

Found %: C 72.30; H 9.57; N 11.10. $C_{15}H_{24}ON_2$. Calculated %: C 72.52; H 9.75; N 11.28.

A picrate was prepared by the usual method; it formed yellow needles with m.p. 179-180° (decomp.; from ethanol). The perchlorate formed plates with m.p. 233-234° (decomp.).

1.8 g of aphylline hydrochloride was heated for 30 minutes at 250-265°. The reaction mixture was dissolved in 10 ml of dilute hydrochloric acid and extracted with ether after being made alkaline. Evaporation of the ether gave 1 g of a yellow oil, from which substance B was obtained by the method described above.

SUMMARY

1. The crystalline substance, which separates during the production of anabasine sulfate, consists mainly of aphyllinic acid sulfate, formed during the production process by the action of sulfuric acid on aphylline.

2. Aphyllidinic acid was prepared and described for the first time.

3. The possibility of obtaining aphylline in quite good yield by heating aphyllinic acid to melting was demonstrated.

4. In investigating the product obtained by melting aphyllinic acid hydrochloride, a crystalline substance was isolated, which was isomeric with aphylline. The same substance was obtained by melting aphylline hydrochloride.

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STEROID SAPOGENINS

III. THE SAPOGENINS OF THE RHIZOMES AND LEAVES OF YUCCA FILAMENTOSA FROM THE BLACK SEA COAST OF CAUCASIA

O. S. Madaeva

The literature contains extensive material on the study of the composition of sapogenins obtained by hydrolyzing saponins, extracted from various types of yuccas [1-10]. We investigated the rhizomes and leaves of Yucca Filamentosa from the Black Sea coast of Caucasia, which were given to us by the All-Soviet Institute of Medicinal and Aromatic Plants (VILAR).

It is known [5] that examples of this type of yucca are outstanding in the differences in composition of the sapogenins obtained. 1.1% of gitogenin [9] was isolated from the rhizomes of Y. filamentosa growing in California; in addition to gitogenin, tigogenin and traces of mexogenin were extracted from leaves collected in southern France [4] and, finally, the Czech scientist Cerny [10], whose work was carried out at almost the same time as ours, reported that the leaves of Y. filamentosa growing in Czechoslovakia, yielded 0.72% of tigogenin.

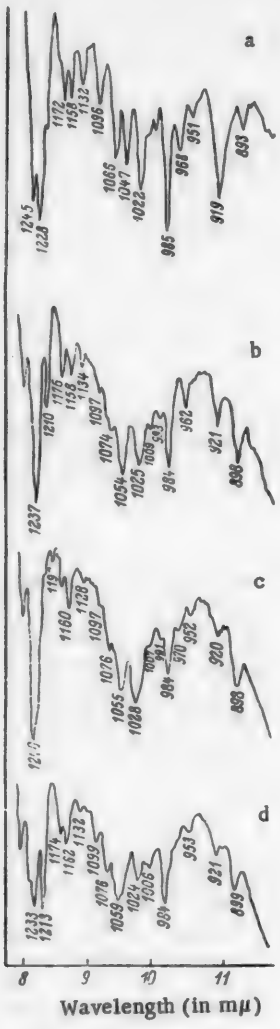
We extracted and hydrolyzed the saponins from the rhizomes of Y. filamentosa (collected in the autumn of 1953 in Tsikhisdziri) basically by Wall's method [11], substituting methanol for ethyl alcohol in the extraction; the aqueous, fat-free solution of the saponins gave a colored, friable precipitate which was the water-insoluble saponins. The results of the detailed study of the nature of the water-insoluble saponins obtained will be reported separately.

The aqueous saponin solution was extracted with butanol to free it from sugars and traces of protein. After distilling off the butanol, the aqueous solution was hydrolyzed with 4 N hydrochloric acid. The sapogenin mixture was washed with cold alcohol and light petroleum ether and formed a white, crystalline precipitate, whose chloroform solution did not give a yellow color with tetranitromethane, indicating that the sapogenins had a saturated character. After chromatography on aluminum oxide and repeated recrystallization, this mixture yielded a precipitate which in elementary composition, melting point and R_f corresponded to sarsasapogenin (I); the acetate obtained had an IR-spectrum characteristic of sarsasapogenin acetate [12] (see figure, curve a), and corresponded to it in elementary composition. It is known [13] that sapogenins of similar polarity cannot be separated clearly on aluminum oxide; thus the separation of a second monohydroxysapogenin was quite difficult but these difficulties were eliminated by using paper partition chromatography extensively. The eluates containing the same sapogenins were separated by the results of paper chromatography. The chromatograms of the last eluates gave two large spots – one in the region of ketosapogenin, which was closer to the starting line, and the other spot corresponded to the less polar, saturated monohydroxysapogenin. Using Girard T reagent, two sapogenins were isolated from this mixture and identified as tigogenin (II) and hekogenin (III); their acetates were prepared and compared with appropriate samples of pure sapogenins. The IR-spectrum of tigogenin acetate, of which a small amount was obtained, coincided completely with the IR-spectrum of authentic tigogenin acetate [13] (see figure, curve b).

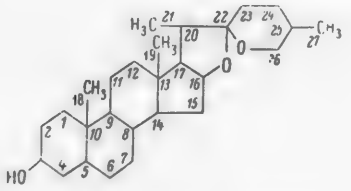
It should be noted that an attempt to separate the sapogenins from the rhizomes of Y. filamentosa without purifying the saponins with butanol, resulted in strong carbonization during hydrolysis and the sapogenins could not be obtained practically.

Saponins were also extracted from the leaves of Y. filamentosa (collected in March 1955 in Kobulet) in a Soxhlet apparatus with 80% methanol and defatted with dichloroethane. Sapogenins isolated from saponins that

had been purified with butanol were less tarry than those from saponins not treated with butanol. However, a pure sapogenin could not be obtained by recrystallization: apparently this was due to the traces of other sapogenins, which were later detected chromatographically. To isolate and purify the sapogenins chromatographically we checked the conditions proposed by Wall [13, 14] and Cerny [10]. A comparison of the chromatographic results showed that, using the second method, developed by the Czech scientist (elution with ether), resulted in the separation of the monohydroxysapogenins from the tarry impurities, while in using the first method (washing with chloroform, a more polar solvent), the tarry impurities came out with the monohydroxysapogenins. The residues from the ether eluates gave pure tigogenin after one recrystallization, while the recrystallized tigogenin, isolated from the chloroform eluates, had a lower melting point.



Infrared absorption spectra of sapogenin acetates. a) Sarsasapogenin acetate; b) tigogenin acetate; c) chlorogenin diacetate; d) smilagenin acetate.



I) Sarsasapogenin – 5β,25 L-spirostan-3β-ol [11];
II) tigogenin – 5α,25 D-spirostan-3β-ol;
III) hekogenin – 5α,25 D-spirostan-12-one,3β-ol;
IV) gitogenin – 5α,25 D-spirostan-2α,3β-diol;
V) chlorogenin – 5β,25 D-spirostan-3β,6β-diol;
VI) smilagenin – 5β,25 D-spirostan-3β-ol.

After isolation of the tigogenin the column was eluted with methanol; the crystalline precipitate obtained from the methanol eluates, when chromatographed on paper with solvents for sapogenins of group I [15], gave one spot near the starting line; according to the R_f value it could belong to a dihydroxysapogenin. A comparison of the chromatogram of this substance with those of pure samples of gitogenin (IV) and chlorogenin (V) showed that it gave a spot which had an R_f value identical to that of chlorogenin. The IR-spectrum of its acetylation product was identical to the IR-spectrum of chlorogenin diacetate (see figure, curve c); in addition, the appearance of a yellow color when a drop of concentrated sulfuric acid was added was further proof that it was chlorogenin, as under these conditions gitogenin gave a purple color [16]. After recrystallization of tigogenin from a mixture of benzene and hexane (1 : 1), the residue from the filtrates gave a tarry residue when chromatographed on a column with aluminum oxide; this tarry residue gave one spot on the chromatogram with a greater R_f value than that of tigogenin. After acetylation, its IR-spectrum had bands characteristic of smilagenin acetate (VI; curve d).

The IR-absorption spectra were obtained in the physical chemistry laboratory under the supervision of Iu. N. Sheinker and we would like to thank him.

EXPERIMENTAL

For paper chromatography we mainly followed the method in [15], which had been changed slightly [17].

The work was carried out with rhizomes and leaves, which had been dried in air. These were ground and passed through a sieve with 3 mm holes.

Isolation of sapogenins from rhizomes of Y. filamentosa. 600 g of ground rhizomes were exhaustively extracted with 80% methanol in a Soxhlet apparatus for 3 days (a test of the residual plant material for hemolysis was negative). The methanol was distilled off and an equal volume of alcohol added to the residue, which was extracted with benzene, saturated with 50% alcohol. The alcohol was distilled off from the aqueous alcohol solution of the saponins; on standing the residue gradually deposited a precipitate of the water insoluble saponins. The precipitate was filtered off and washed with water; it did not dissolve in ether, dissolved slightly in alcohol and more so in hot butanol and did not deliquesce in air. Drying at 100° yielded 5.4 g of a fine, reddish powdery precipitate. The precipitate was not examined further; it was only hydrolyzed with acid. Paper chromatography of the sapogenins obtained gave only a spot with an R_f in the region of monohydroxysapogenins.

After hydrolysis of the water soluble saponins, freed from sugars by extraction with butanol, we obtained 8.5 g of a light yellow, tarry residue, which completely crystallized on being ground with alcohol. When washed with cold alcohol and petroleum ether, it became almost colorless; the m.p. was 178-182°. For purification 2.7 g of this precipitate was dissolved in 50 ml of dry benzene (thiophene free), containing 2% chloroform, and chromatographed on 38 g of aluminum oxide. The column was eluted using a gradually increasing chloroform content and then with chloroform alone. After several recrystallizations from methanol, ether and acetone, the residue isolated from the chloroform eluates corresponded to sarsasapogenin (I) in R_f value. The m.p. was 197-199°; literature data: m.p. 199-200°, 200° [11, 18].

Found %: C 77.79; H 10.36. $C_{27}H_{44}O_3$. Calculated %: C 77.80; H 10.6.

Sarsasapogenin acetate. 1.5 g of impure sapogenins with m.p. 180-183°, 2.5 ml of pyridine and 12 ml of acetic anhydride were boiled for 30 minutes. A precipitate formed after cooling; the liquid was removed from it and the precipitate was washed with water, dried and recrystallized twice from methanol and then from acetone. The m.p. was 143-144°, $[\alpha]^{20}D$ −72° (c 1; $CHCl_3$); literature data: m.p. 128-130° [15], 138-142° [1], 144-145° [11], $[\alpha]^{20}D$ −71° ($CHCl_3$) [15].

Found %: C 75.84, 75.81; H 10.01, 10.00. $C_{29}H_{46}O_4$. Calculated %: C 75.94; H 10.11.

Tigogenin (II). 5 g of the mixture of sapogenins with m.p. 178-181° was dissolved in 100 ml of chloroform, placed in a column of 105 g of aluminum oxide and washed with 65 ml portions of chloroform to give 52 eluates. On paper, the first 7 eluates showed only a spot close to the solvent front; it was not possible to identify a substance from them. The following 10 eluates gave two spots – one on the level of the spot from the first seven eluates and the second corresponding to sarsasapogenin (R_f 0.89; total weight of residues, 0.7 g). On the chromatograms of the 18th to the 40th eluates were found three spots – two spots on the levels of the spots of the previous eluates and the third corresponding to tigogenin (R_f 0.71; total weight of residues of these eluates, 1.2 g). We were unable to isolate pure tigogenin from these by crystallization. The last eluates (from the 41st to the 52nd) gave two spots – one large one with R_f 0.71 and the second, a new one close to the starting line with R_f 0.34; from its position it corresponded to a ketosapogenin (total weight of residues, 2 g). Further washing of the column with chloroform with methanol added gave a tarry solution; its paper chromatogram showed that it contained a mixture of the sapogenins found above. These residues were not examined.

1.75 g of the residues of the combined eluates from 41 to 50 was treated with Girard T reagent. From the nonketonic fraction we obtained 1.16 g of a yellowish residue, which was washed with ether. After recrystallization from acetone the substance had m.p. 198-202°; R_f 0.71, like the sample of tigogenin from the Prague Chemical Institute of the Czechoslovakian Academy of Sciences; a mixed melting point was not depressed. Literature data: m.p. 201-202° [15], 206 [18]. The tigogenin acetate obtained from it had m.p. 202-204°; literature data: 195-197° [15], 206-208° [11]. The IR-spectrum corresponded to the IR-spectrum of tigogenin acetate [13].

Hekogenin (III). The aqueous solutions after the separation of the nonketonic fraction was acidified with hydrochloric acid to give 0.5 g of a slightly colored precipitate, which had m.p. 254-258° after two recrystallizations from acetone and then one from ethyl acetate. A paper chromatogram showed a spot identical in R_f value to a

sample of pure hekogenin; a mixed melting point with hekogenin, isolated from Agave Americana (see report V) was not depressed. Literature data: m.p. 245, 253, 268° [1] and 245-247° [15]. The hekogenin acetate had m.p. 243-245°; literature data: 243°, 252° [1], 245° [11]. Its IR-spectrum was in complete agreement with the IR-spectrum of hekogenin acetate [12]. In elementary analysis it corresponded to hekogenin acetate.

Isolation of sapogenins from the leaves of Y. filamentosa. 220 g of powdered leaves was extracted in a Soxhlet apparatus with 80 % methanol; dichloroethane was used for defatting. After hydrolysis with 3 N hydrochloric acid and subsequent saponification with alcoholic alkali, 3.14 g of a tarry substance was obtained. Half of this (1.57 g) was chromatographed by Wall's method [13, 14] and from the chloroform eluates we obtained 1.2 g of a crystallizable oil, which was treated with ethyl acetate to give 0.42 g of crystals with m.p. 197.5-203°. The residue from the column was removed by elution with benzene, containing 30% alcohol. The second half of the tarry product (1.57 g) was chromatographed under the conditions described by Cerny [10]. The ether eluates yielded 1.01 g of a tarry residue, which gave 0.37 g of a solid with m.p. 202-204° after recrystallization. Paper chromatography of it gave one spot with R_f 0.71 and the filtrates from the recrystallization gave two spots – one with R_f 0.71 and a second with a larger R_f value. The residue from the column was washed out with a mixture of ether and alcohol. Tigogenin acetate, prepared from the tigogenin, was crystallized from acetone and washed with petroleum ether. The m.p. was 202-204°, $[\alpha]^{20}D$ −68.3°, −71° (c 1; $CHCl_3$); literature data: m.p. 204°, $[\alpha]^{20}D$ −73° [18]; m.p. 202-204°, $[\alpha]^{20}D$ −69° ($CHCl_3$) [10].

Found %: C 76.02; H 10.02. $C_{29}H_{48}O_4$. Calculated %: C 75.94; H 10.11.

SUMMARY

1. 0.45% of a mixture of sapogenins, consisting of sarsasapogenin, tigogenin and hekogenin was extracted from the rhizomes of Yucca filamentosa from the Black Sea coast of Caucasia.

2. 0.34% of tigogenin was obtained from the leaves of Y. filamentosa and it was shown that the leaves also contain chlorogenin and smilagenin.

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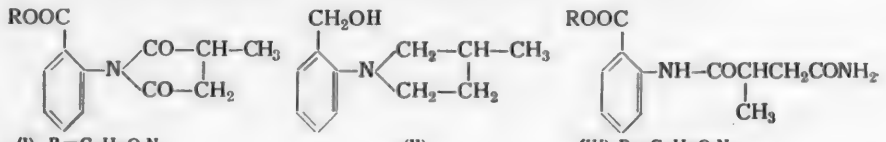
INVESTIGATION OF ACONITE ALKALOIDS

X. ELATINE. STRUCTURE OF ESTERIFYING ACID

A. D. Kuzovkov and A. V. Bocharnikova

Hydrolytic cleavage of the alkaloid elatine gives the aminoalcohol elatidine [2] and methylsuccinylanthranilic acid [3]. In report (IV) [3], one of us proposed that in the molecule of elatine the carboxyls of methylsuccinic acid and the nitrogen of anthranilic acid formed an N-substituted methylsuccinimide grouping. On this basis, the partial formula (I) was proposed for elatine. We confirmed this proposal by studying the reduction of elatine with lithium aluminum hydride; in addition to elatidine, we obtained the base (II) with the composition $C_{12}H_{17}ON$, which was formed from elatine by reductive cleavage of one of the ester links and reduction of the two carbonyls of the methylsuccinyl group to methyl groups, which indicated [4] the presence of amide carbonyls in the esterifying acid of elatine. The reduction of elatine proceeded by the equation (I) $\longrightarrow$ (II) + elatidine.



(I) R = $C_{25}H_{43}O_6N$; (III) R = H

(II)

(IV) R = $C_{25}H_{41}O_6N$

The base $C_{12}H_{17}ON$ may only be 2-[N-(3-methylpyrrolidyl)]-benzyl alcohol (II) and the esterifying acid, consequently, has the formula (III). The acid structure corresponding to formula (III) was also proposed for the esterifying acid of the alkaloid methyllycaconitine by Cookson et al., [5] on the basis of spectrographic investigations. This work was carried out at the same time as our investigation of elatine.* The similarity of elatine and methyllycaconitine had been noted by us previously [3]. Apparently these alkaloids differ only in that elatine contains a dihydroxymethylene group instead of the glycol group of methyllycaconitine. By reduction of methyllycaconitine with lithium aluminum hydride, we obtained a base $C_{12}H_{17}ON$, identical with the base (II), obtained by the reduction of elatine. This confirmed the data of Cookson et al. on the structure of the esterifying acid of methyllycaconitine.

The presence of a substituted methylsuccinimide group in elatine and methyllycaconitine explains their instability towards ammonia and the ease of conversion [6] or methyllycaconitine into delsemine (IV). It is similar to the conversion of succinimide into succinamide [7]. The isolation of elatine and methyllycaconitine from plants has to be carried out without the use of ammonia. Thus, for example, the extraction of elatine with xylene from the plant Delphinium elatum, wetted with 5% soda solution, raises the yield of the alkaloid from 0.03 [2] to 0.15%. Methyllycaconitine hydroiodide may be obtained from Delphinium dictyocarpum D. C. [8]. Extraction with dichloroethane after wetting the dry plant with soda solution raised the yield to 0.7%; if ammonia is used as the alkali, delsemine may also be isolated from the combined alkaloids in addition to methyllycaconitine.

The similarity in the structure of elatine and methyllycaconitine causes the similarity in their pharmacological properties: both of them are curare-like preparations [9]; they also have an effect when administered internally and in this they are superior to curare-like substances containing quaternary nitrogen atoms. The curare-like pro-

*Our fourth report [3] was received by the editor of the journal on April 23, 1954, and the work of Cookson et al., [5] in May, 1954.

perties are not connected with the presence of the succinimide group in the molecule of these alkaloids as these properties are also possessed by delsemine [10], avadkharidine* and ajacine.* Apparently, curare-like properties are inherent in esters of lycoctonine or amino alcohols close to it, esterified with N-acylated anthranilic acid.

EXPERIMENTAL

Reduction of elatine. 4 g of elatine was placed in the thimble of a Soxhlet apparatus and a solution of 2 g of $LiAlH_4$ in 0.5 liter of absolute ether in the flask of the apparatus. The elatine was extracted for about 60 hours and then the reaction mixture was treated with excess 10% hydrochloric acid. The ether layer was extracted 3 times with 10% hydrochloric acid. The acid extracts were combined and made alkaline with NaOH with cooling until the aluminum hydroxide dissolved. The base was extracted from the alkaline solution with chloroform. After drying the extract with sodium sulfate and evaporating off the solvent, we obtained 3.5 g of a mixture of bases, from which elatidine crystallized when ether was added; the yield was 2.3 g. The solvent was removed from the mother liquors and the residue vacuum distilled to give 2-[N-(3-methylpyrrolidyl)]-benzyl alcohol; the yield was 0.7 g.

B.p. 105-108° (0.1 mm), d^{20}_4 1.0799, $n^{20}D$ 1.5652, MR 57.7; calc. 57.3; $[\alpha]^{20}D$ +8.6° (c 2.8 in alcohol).

Found %: C 74.78; H 8.97; N 7.5; labile hydrogen 0.52. $C_{12}H_{17}ON$. Calculated %: C 75.36; H 8.96; N 7.35; labile hydrogen 0.53.

The picrate of 2-[N (3-methylpyrrolidyl)]-benzyl alcohol was prepared by mixing alcohol solutions of the base and picric acid and the salt was washed with alcohol on the filter and dried, when it had m.p. 103°.

Reduction of methyllycaconitine. 10 g of the base was dried by distillation of benzene from it and then it was dissolved in 0.5 liter of absolute ether and reduced with 4 g of $LiAlH_4$ (2 hours boiling). The mixture of bases, isolated like the reduction products of elatine, were dissolved in moist ether; at this lycoctonine cyrstallized and after drying it had m.p. 149° (in vacuum). It did not depress the melting point of a sample of lycoctonine, obtained by saponification of the alkaloid. From the mother liquor we isolated 1.6 g of 2-[N-(3-methylpyrrolidyl)]-benzyl alcohol.

B.p. 108° (0.1 mm), d^{20}_4 1.0726, $n^{20}D$ 1.5678, $[\alpha]^{20}D$ +12.60° (c 2.5, in alcohol). The picrate had m.p. 104° and did not depress the melting point of the substance obtained from elatine.

SUMMARY

The esterifying acid of elatine and methyllycaconitine is 2-[N-(3-methyl-2,5-dioxopyrrolidyl)]-benzoic acid. The presence of a substituted succinimide group explains the instability of elatine and methyllycaconitine to ammonia.

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* According to data obtained by colleague, P. M. Dozortseva, at the All-Soviet Chemical Pharmaceutical Research Institute. "Avadkharidine" - as in original.

** See C. B. Translation.

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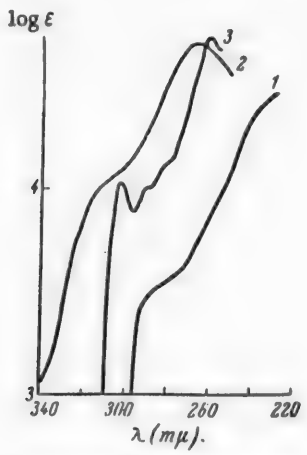
INVESTIGATION OF ACONITE ALKALOIDS

XI.* OXIDATION OF THE HYDROCARBON $C_{18}H_{18}$, FORMED DURING DEHYDROGENATION OF ZONGORINE **

A. D. Kuzovkov

The hydrocarbon $C_{18}H_{18}$ was obtained previously [2] in the dehydrogenation of zongorine with selenium and a hypothesis was put forward that this hydrocarbon was a trialkylphenanthrene. To find the position of the alkyl groups in hydrocarbon $C_{18}H_{18}$, it was oxidized with potassium ferricyanide under the conditions used by Ruzicka et al., [3] for oxidizing retene to a mixture of phenanthrenedicarboxylic-1,7 acid and diphenyltetracarboxylic--2,3,2',4' acid. When oxidized, hydrocarbon $C_{18}H_{18}$ also gave two acids which were isolated in the form of their methyl esters: ester (I) $C_{20}H_{18}O_8$, m.p. 150.5-151°; ester (II) $C_{20}H_{16}O_6$, m.p. 227-229°.



Ultraviolet absorption spectra (in alcohol). 1) Ester (I), methyl ester of diphenyltetracarboxylic--2,3,2',4' acid; 2) ester (II), methyl ester of phenanthrene-tricarboxylic-1,7,9 (or 10) acid; 3) hydrocarbon $C_{18}H_{18}$.

In composition ester (I) corresponds to the methyl ester of a diphenyltetracarboxylic acid. The melting point of the ester coincides with that of the dimethyl ester of diphenyltetracarboxylic-2,3,2',4' acid. For comparison, the latter substance was synthesized by known methods: β-methylnaphthalene was converted to 1,7-dimethylphenanthrene [4], which was oxidized to diphenyltetracarboxylic-2,3,2',4' acid [3]. The methyl ester of this acid was identical to ester (I).

The infrared spectrum of ester (II) has a band, characteristic of ester carbonyl groups (1720 cm^{-1}); there are no hydroxyl group and keto group bands. One can conclude from this that all six oxygen atoms, in a molecule of the substance, belong to carbomethoxy groups. The composition of ester (II) corresponds to that of an ester of a phenanthrenetricarboxylic acid.

The character of the ultraviolet absorption of ester (I) (figure) indicates the presence of a closed phenanthrene nucleus in this substance. In going from hydrocarbon $C_{18}H_{18}$ to the ester of diphenyltetracarboxylic-2,3,2',4' acid, there is a sharp decrease in the absorption intensity, because of the destruction of the system of conjugated bonds of the phenanthrene nucleus. Ester (I) absorbs light more strongly than hydrocarbon $C_{18}H_{18}$ which indicates that the system of conjugated bonds of the phenanthrene nucleus remains and that a new conjugation of the nuclear double bonds with the carbonyl groups appears.

The results of oxidation confirm the hypothesis that hydrocarbon $C_{18}H_{18}$ is a trialkylphenanthrene; they also indicate that the alkyl groups in hydrocarbon $C_{18}H_{18}$ are in positions 1,7 and 9 or 10 of the phenanthrene nucleus.

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*See [1] for previous report.

**"Zongorine" - as in original Russian text.

as only in this case can diphenyltetracarboxylic-2,3,2',4' acid be formed in addition to the phenanthrenetricarboxylic acid.

Phenanthrene hydrocarbons with substituents in positions 9 or 10 have not been detected up to now in the substances formed by the dehydration of aconite alkaloids. The detection of an alkyl group in hydrocarbon $C_{18}H_{18}$ in position 9 or 10 of the phenanthrene nucleus indicates either the presence of a substitutent in the corresponding nucleus in zongorine, or that this nucleus is seven- or eight-membered. During dehydrogenation such rings may be converted [5] into six-membered aromatic systems with new alkyl groups appearing at the contracted rings; the conversion may be facilitated by the presence of quaternary carbon atoms and a double bond in the molecule.

EXPERIMENTAL

0.5 g of hydrocarbon $C_{18}H_{18}$ and a solution of 100 g of potassium ferricyanide and 7 g of potassium hydroxide in 250 ml of water was heated and stirred at 90°. After being heated for 30 hours, the reaction mixture was treated with 40 g of potassium ferricyanide and 7 g of potassium hydroxide; heating and stirring were continued; after another 30 hours, a further 20 g of oxidant and 7 g of alkali were added. The total length of heating was 80 hours. After cooling, the precipitate of salts was filtered off and washed with ether and the filtrate extracted with ether. Drying and evaporation of the ether extract yielded about 0.05 g of unchanged hydrocarbon. The aqueous solution was acidified with hydrochloric acid. By extraction with ether, we obtained about 0.5 g of a crystalline mixture of acids, which was separated into two parts by trituration with methanol at room temperature: a)— insoluble in methanol (0.1 g) and b)— soluble in methanol (0.4 g). Esterification of part(a)with diazomethane in ether gave ester (II). For crystallization, the substance was dissolved in a small amount of chloroform and an equal volume of methanol added to crystallize out 50 mg of ester (II) with m.p. 227-229°.

Found %: C 68.20; 67.96; H 4.65, 4.52. $C_{20}H_{16}O_6$. Calculated %: C 68.18; H 4.58.

Part(b)was also esterified with diazomethane in ether solution. The reaction product was recrystallized from a large volume of methanol and this gave a small amount of ester (II). Evaporation of the mother liquor yielded a substance with m.p. 149-150°; after recrystallization of the latter from methanol, we obtained 15 mg of ester (I) with m.p. 150.5-151°.

Found %: C 62.02; H 4.79. $C_{20}H_{12}O_8$. Calculated %: C 62.20; H 4.70.

Ester (I) did not depress the melting point of the methyl ester of diphenyltetracarboxylic-2,3,2',4' acid. The two substances had identical infrared spectra.

SUMMARY

1. Oxidation of hydrocarbon $C_{18}H_{18}$ gave phenanthrenetricarboxylic-1,7,9 (or 10) acid and diphenyltetracarboxylic-2,3,2',4' acid.

2. It was shown that hydrocarbon $C_{18}H_{18}$ is a trialkylphenanthrene containing alkyl groups in positions 1,7 and 9 or 10 of the phenanthrene nucleus.

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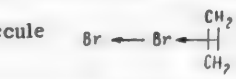
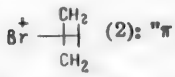
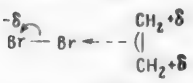
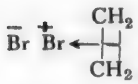
*Original Russian pagination. See C. B. Translation.

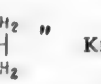
A DISCUSSION

IN REPLY TO THE "REMARKS" BY E. A. SHILOV [1]

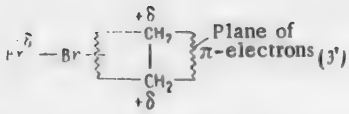
A. I. Titov and F. L. Makliaev

First of all the "Remarks" by E. A. Shilov should have been published in the Ukrainian Chemical Journal in 1955. In the original form of the article, E. A. Shilov wrote that Dewar [2] had considered a complex of an olefin and a halogen molecule  (1). as an intermediate product. In our "Reply," it was stated that actually in the article quoted, Dewar had written only of the bromine cation adduct with the hypothetical formula  (2): "π-complex in which bromine cations are linked to the π-electrons" [3]. E. A. Shilov is mistaken in identifying formula (2) with the structure we proposed for the complex of a halogen molecule with the olefin  (3). After receiving our answer E. A. Shilov gave a second variation of Dewar's complex,  (4), trying as before, to make formula (4), at least superficially similar to our formula (3), and not noticing that the independent existence of the ions makes formula (4) and (2) identical.

In connection with this, we also changed our reply somewhat. In spite of the fact that both articles were quite ready, they were not published and E. A. Shilov preferred to send a third variation of "Remarks" to J. Gen. Chem.

The similarity we noted between the formula of Dewar's hypothetical cations of type (2) and the Roberts-Kimbal formula, (5), contrary to E. A. Shilov's opinion, is accepted by the majority of chemists. In particular, Dewar himself wrote [2]: "thus in the addition of bromine to a double bond the cyclic intermediate is probably  " Knuniants, Kabachnik [4] et al., even assigned the Roberts-Kimbal structure directly to the π-complex. The similarity between these formulas consists basically of the fact that they represent an adduct, in which a bromine cation is chemically bonded to both carbon atoms of ethylene.

In our work carried out in 1943-46 [5, 6], with which E. A. Shilov is not familiar, complexes of halogen molecules with olefins were assumed to be the intermediate products of conjugated addition. The structure of these complexes we then represented as fully as possible by formula (3'), at which we arrived independently of Dewar's views.



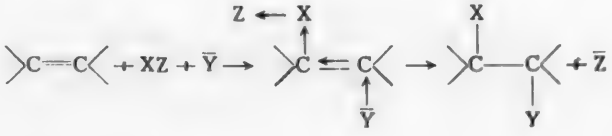
(3')

Its basic idea is identical to that of the more recent and concise formula (3), as both express the reaction caused by the introduction of π -electrons into the sphere of an electrophilic halogen molecule. The curve in formula (3) reflects the eccentric disposition of the density of π -electrons and their weaker bond to C nuclei, on which the peculiarities of the properties of the unsaturated compounds depend, and the sign ⟵ underlines the weak donor--acceptor bond of Br_2 and C_2H_4 in the complex; the correlation between the symbol for the semipolar bond and the sign ⟵ is approximately the same as that between the dash and the dotted line in the classical theory of valence. The use of a valence dash by Dewar to represent the bonds of the already generalized ethylene electrons, even with a cation, is incorrect; structure (1) and the formula given by E. A. Shilov for the adduct of HBr and ethylene [1] contradict even more the theory of valence and the symbols generally accepted. Other authors, in particular, O. A. Reutov [7] when discussing E. A. Shilov's results, have also concluded that it was advantageous to use the sign ⟵ for expressing the bonds of electrophilic molecules with π -electrons. Our ideas on the chemical nature of the initial reaction of olefins with halogens have now been confirmed by many other investigations [8].

We will not examine the similarity and difference between our mechanism of conjugated addition and one of Robinson's schemes, for the sake of brevity and also as two years ago [9] he expressed completely different views on the course of the reaction of bromine with ethylene, which have very little in common with the theory of conjugated addition. Naturally, features may be found in our ideas similar to the hypotheses of other authors, starting with Dumas (etherin theory), Lavoisier (murium hypothesis), Tile and finally Dewar.

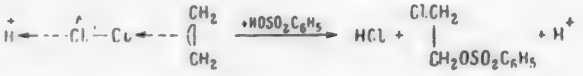
The idea introduced by us [5, 6] of "conjugated addition reactions" agrees with the facts observed – the drawing in of a third component into the reaction is related to the reaction of the halogen with the olefin. According to present day theory, the mechanism of conjugated reactions is actually characterized by the formation of labile complexes that react with a third component [10]. For differentiation, the type of process being examined may be defined, according to A. N. Nesmeianov [11], as the conjugated addition of halogens to olefins.

In our interpretation of the mechanism of conjugated addition of halogens to olefins [5, 6], the moving force of the reaction is clearly expressed as the formation of an electrophilic complex of a halogen molecule with the olefin, which is absent from the formal concept of E. A. Shilov of trimolecular coordinated reactions [12].



(6)

Starting with such a concept, it is doubtful if one could deduce that the strongest anhydrous acids could be involved in the reaction of halogens with olefins



(7)

and, besides that, with greater success than the acids' salts. These reactions illustrate the unusually high alkalation capacity of complexes of halogens with olefins, which we first proved. They can in no measure be used as examples of the applicability of E. A. Shilov's scheme.

E. A. Shilov denies the possibility of the activating effect of sulfuric acid on the reaction of an aromatic nucleus with a halogen molecule, but this has been observed by many authors and should be considered as quite natural for all protonic and aprotonic acids. E. A. Shilov considers that the substitution of hydrogen atoms at π -bonds proceeds by a radical mechanism, but this is also baseless as it is contradicted, for example, by the extensive material on the chemistry of aromatic compounds. Without doubt, the conditions and results of the reactions we investigated correspond completely with the ionic mechanism assigned to them, and among them those for the side reaction of

hydrogen substitution. We have not examined the mechanism of the reaction of acetylene on the surface of solid mercuric chloride and E. A. Shilov's remarks on this subject do not contradict our ideas and even enlarge somewhat the range of conjugated addition reactions. E. A. Shilov's objection to the use of letter coefficients for denoting chemical activity is best refuted by the fact that they are used, in particular, f, in work on reactivity; however, as is known, the meaning of the coefficient is determined not by its transcription but by the content.

In conclusion one must state that the first reason for E. A. Shilov's "Remarks" was an error. This error led him, as the above shows, to a series of baseless statements. Our contribution to the theory of conjugated addition, in particular, the substantiation of the probable role in them of complexes of halogen molecules with olefins, a rational exposition of their chemical structure, the illustration of the extremely high alkylation capacity of the complexes (even reacting with the strongest acids), the discovery and explanation of the orientation rules in conjugated additions, proof of the absence of a preliminary reaction of halogens with the third component etc., were ignored by E. A. Shilov and to belittle the synthesis achievements he called them preparative. Such results are rarely found in any, even prolonged, investigations on the reactions of halogens with olefins.

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**In Russian.

SIGNIFICANCE OF ABBREVIATIONS MOST FREQUENTLY ENCOUNTERED IN SOVIET PERIODICALS

FIAN	Phys. Inst. Acad. Sci. USSR.
GDI	Water Power Inst.
GITI	State Sci.-Tech. Press
GITTL	State Tech. and Theor. Lit. Press
GONTI	State United Sci.-Tech. Press
Gosenergoizdat	State Power Press
Goskhimizdat	State Chem. Press
GOST	All-Union State Standard
GTTI	State Tech. and Theor. Lit. Press
IL	Foreign Lit. Press
ISN (Izd. Sov. Nauk)	Soviet Science Press
Izd. AN SSSR	Acad. Sci. USSR Press
Izd. MGU	Moscow State Univ. Press
LEIIZhT	Leningrad Power Inst. of Railroad Engineering
LET	Leningrad Elec. Engr. School
LETI	Leningrad Electrotechnical Inst.
LETIIZhT	Leningrad Electrical Engineering Research Inst. of Railroad Engr.
Mashgiz	State Sci.-Tech. Press for Machine Construction Lit.
MEP	Ministry of Electrical Industry
MES	Ministry of Electrical Power Plants
MESEP	Ministry of Electrical Power Plants and the Electrical Industry
MGU	Moscow State Univ.
MKhTI	Moscow Inst. Chem. Tech.
MOPI	Moscow Regional Pedagogical Inst.
MSP	Ministry of Industrial Construction
NII ZVUKSZAPIOI	Scientific Research Inst. of Sound Recording
NIKFI	Sci. Inst. of Modern Motion Picture Photography
ONTI	United Sci.-Tech. Press
OTI	Division of Technical Information
OTN	Div. Tech. Sci.
Stroiizdat	Construction Press
TOE	Association of Power Engineers
TsKTI	Central Research Inst. for Boilers and Turbines
TsNIEL	Central Scientific Research Elec. Engr. Lab.
TsNIEL-MES	Central Scientific Research Elec. Engr. Lab.–Ministry of Electric Power Plants
TsVTI	Central Office of Economic Information
UF	Ural Branch
VIESKh	All-Union Inst. of Rural Elec. Power Stations
VNIIM	All-Union Scientific Research Inst. of Meteorology
VNIIZhDT	All-Union Scientific Research Inst. of Railroad Engineering
VTI	All-Union Thermotech. Inst.
VZEI	All-Union Power Correspondence Inst.

Note: Abbreviations not on this list and not explained in the translation have been transliterated, no further information about their significance being available to us. – Publisher.